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AN EVALUATION OF CURARE IN SPASTICITY DUE TO SPINAL-CORD INJURIES*

ROBERT A. KUHN, M.D.,† AND DONALD S. BICKERS, M.D.‡

FRAMINGHAM, MASSACHUSETTS

IN 1850 Claude Bernard[1] demonstrated the site of action of curare to be the neuromuscular junction. His experiments have been verified by numerous investigators, and in 1935 West[2] and King[3] clarified the mode of action and enumerated the pharmacologic properties of the drug. It was not until 1943 that Wintersteiner and Dutcher[4] crystallized the quaternary ammonium salt, d-tubocurarine chloride. Recent availability of this pure preparation has stimulated clinical and pharmacologic investigations.

The gross effects of curare on the normal human subject have been thoroughly investigated. The intrinsic musculature of the toes and eyes demonstrates early paresis, which successively involves the muscles of the limbs, head and neck. Intercostal muscle relaxation is soon followed by paralysis of the diaphragm. During the early stages of curarization, the patient complains of blurring and fuzziness of vision. The eyelids droop, diplopia develops, and the jaws relax. There is weakness and heaviness of the neck muscles progressing to head drop. Further administration of the drug produces complete peripheral paralysis and, finally, respiratory arrest.[5] These signs and symptoms disappear in reverse order, and the rate of disappearance is dependent upon the nature of the curare preparation administered.

Although it is known that curare exerts its influence primarily at the myoneural junction, the exact mode of action remains in doubt. Eccles, Katz and Kuffler[6–10] demonstrated that the endplate potential in fully curarized muscle rises to subthreshold levels and subsides without initiating muscle response. The size of the potential — that is, the degree of depolarization — depends in part on the concentration of the curare in the muscle. The degree of block is controllable, and certain frequencies can be suppressed. This action may well explain obliteration of various involuntary movements while normal voluntary contractions continue.[11]

Clinically, curare has been used with value in a number of conditions necessitating muscle relaxation. Curare therapy of tetanus has met with some success,[12–15] and convulsions incident to shock therapy are effectively diminished.[16–18] However, it is in anesthesiology that this drug has achieved its maximal usefulness to date. In 1942, Griffith[19] reported the use of curare as an adjuvant to general anesthesia, and numerous excellent studies in succeeding years have thoroughly established its value in this field.[20–25]

In 1942 Denhoff and Bradley[26] conducted a controlled study of the effectiveness of aqueous curare in relieving the spasms of children with cerebral diplegia. They concluded that progress under physical therapy was definitely accelerated in these subjects. Muscular relaxation with maximal therapeutic dosages was maintained for a period of approximately four days. Burman,[27] Bennett[28] and Schlesinger[11] reported similar success in patients exhibiting spasticity and rigidity.

Recent reports have indicated that curare might offer valuable aid in the amelioration of spastic paraplegia and paraparesis.[11, 29, 30] Schlesinger[31] administered aqueous curare to 11 patients with extreme spasticity due to spinal-cord injuries and obtained excellent but transient relaxation. A suspension of d-tubocurarine chloride in a peanut-oil and white-wax mixture was prepared in an effort to retard the rate of absorption. The curare effect was found to be prolonged up to three days in some cases, and effective reduction of spasticity§ was not accompanied in any case by unpleasant side reactions. The effect of the curare in oil on patients exhibiting voluntary function masked by spasm seemed more dramatic than that observed in paraplegic patients.

Severe spasm of muscle groups innervated below the level of the cord lesion is frequently a major manifestation of spinal-cord injury, whether due

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The views expressed in this article are those of the authors and do not necessarily represent those of the Veterans Administration.

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§Here, and elsewhere in this article, the term "spasticity" refers to the involuntary muscular contractions occurring in striated muscle groups innervated below the level of the cord lesion. More detailed descriptions of these movements are given in the case reports presented below.

to trauma or to an infectious or neoplastic process. Spasm may be said to be related more or less intimately to the numerous complications following such an injury. Munro[32] has discussed these complications in detail.

Troublesome decubitus ulcers are frequently encountered in patients with cord injuries. These lesions, when present on the heels, knees or hips, are certainly exacerbated by flexion spasms of the lower extremities, and in many cases the continual friction is a major etiologic factor. Prolonged spasticity may lead to permanent contractures of tendons and joints, and neither intensive physiotherapy nor surgery is of much avail. Bladder management is difficult to achieve in these subjects, and the important task of teaching the patient to ambulate

TABLE 1. *Data in Patients with Injuries of Spinal Cord.*

PATIENT	LEVEL OF LESION	DEGREE OF TRANSECTION	INTERVAL SINCE INJURY	DURATION OF SPASMS	TYPE OF SPASM
			days	*days*	
Patients given d-tubocurarine:					
H. B.	2nd dorsal segment	Complete*	805	763	Adductor-flexor, alternating with generalized extensor
E. H.	6th dorsal segment	Partial	740	689	Abductor-flexor, with abdominal and gluteal
D. K.	4th dorsal segment	Complete*	660	618	Extensor, with moderate adductor-flexor
A. K.	3rd dorsal segment	Partial	975	933	Adductor-flexor, with abdominal and gluteal
H. K.	6th dorsal segment	Complete†	858	800	Adductor-flexor, with strong abdominal and gluteal
H. E. K.	7th cervical segment	Partial	661	634	Flexor of upper extremities and extensor of lower extremities
D. L. R.	5th dorsal segment	Complete*	953	933	Adductor-flexor (80 per cent); extensor with abdominal; gluteal (20 per cent).
W. M.	2nd dorsal segment	Complete*	902	857	Flexor and extensor, with abdominal and gluteal
R. Mc.	4th dorsal segment	Complete*	950	715	Adductor-flexor, with abdominal and gluteal
R. N.	5th dorsal segment	Complete*	211	169	Severe adductor-flexor, with mild generalized extensor
A. N.	6th dorsal segment	Partial	706	692	Severe adductor-flexor, with moderate generalized extensor
F. N.	3rd dorsal segment	Complete*	620	590	Alternate adductor-flexor with extensor; abdominal and gluteal.
P. P.	5th dorsal segment	Complete*	749	719	Strong extensor, with moderate adductor-flexor
J. S.	5th cervical segment	Partial	759	719	Adductor-flexor, with abdominal and gluteal
L. S.	10th dorsal segment	Complete*	353	323	Adductor-flexor, with abdominal and gluteal
M. E. S.	6th dorsal segment	Partial	1071	981	Approximately equal adductor-flexor and extensor
R. S.	9th dorsal segment	Partial	494	359	Moderate adductor-flexor, with mild extensor and abdominal and gluteal
Patients given physiologic saline solution:					
R. B.	7th cervical segment	Complete†	232	205	Torsion of trunk and shoulders; mild knee-flexor.
J. C.	3rd dorsal segment	Complete*	777	734	Adductor-flexor, with extensor, abdominal and gluteal
F. C.	5th dorsal segment	Partial	623	593	Adductor-flexor (90 per cent); mild abdominal and gluteal.
J. D.	8th dorsal segment	Complete*	610	568	Adductor-flexor, with abdominal and gluteal
J. Dr.	4th dorsal segment	Complete*	844	814	Adductor-flexor (80 per cent), with mild extensor
L. D.	9th dorsal segment	Complete*	788	604	Dominant adductor-flexor, with mild abdominal and gluteal
H. F.	7th dorsal segment	Complete*	629	610	Severe adductor-flexor, with minimal extensor
T. F. Mc.	5th dorsal segment	Complete*	850	775	Adductor-flexor, with abdominal and gluteal
J. M.	7th dorsal segment	Complete†	668	620	Adductor-flexor, with abdominal and gluteal
W. Mc.	9th dorsal segment	Complete*	800	780	Adductor-flexor, with moderate extensor
R. M.	5th dorsal segment	Complete*	820	790	Adductor-flexor, with adbominal and gluteal
D. P.	5th dorsal segment	Complete*	742	712	Abdominal and gluteal, with flexor-adductor
R. P.	5th dorsal segment	Complete*	741	729	Alternate extensor and adductor-flexor
R. St.	2nd dorsal segment	Complete*	751	709	Abdominal, with plantar-flexor of feet
M. S.	6th dorsal segment	Partial	998	870	Equal, alternate extensor and flexor-adductor
H. W.	7th dorsal segment	Complete*	277	155	Adductor-flexor, with abdominal and gluteal
J. Z.	3rd dorsal segment	Complete*	746	566	Strong extensor, with mild intermittent flexor-adductor

*Anatomic transection of the spinal cord (verified by exploration).
†Physiologic transection of the spinal cord.

effectively is virtually impossible. The person with spasm can be forced into braces, which can be locked in position, but he will never learn the balance that is essential to walking. Pelvic jackknifing, asymmetry of spasms in the lower extremities and the utter unpredictability of onset militate strongly against satisfactory adjustment. The patient becomes wary, loses confidence and resigns himself to a wheelchair life. Unfortunately, only a few patients are able to "tire" their minimal spasms with a short period of exercise or physiotherapy.

TABLE 1 (*Continued*).

DEGREE OF SPASM		DEGREE OF PAIN		REMARKS
BEFORE TREATMENT	AFTER TREATMENT	BEFORE TREATMENT	AFTER TREATMENT	
+++	+++	0	0	No improvement; dizziness on 9th and 13th days.
++++	+	++	+	Marked improvement; moderate relaxation, and drowsiness on 3rd, 5th and 7th days.
++	+	0	0	Questionable improvement; dizziness on 5th, 9th and 21st days.
++++	++++	0	0	Spasms unabated, weakness and diplopia on 5th, 11th, 15th and 17th days.
++++	++++	0	0	Spasms unabated; no symptoms of any type.
++	++	++	++	Spasms unchanged; no symptoms.
+++	++++	+	+	Spasms worse; bitter complaints of visual blurring on 5th, 7th and 9th days.
++	++	+	+	Questionable improvement; headache on 7th and 9th days.
++++	++++	+	+	No symptoms; spasms unabated.
++++	++++	+	+	Severe spasms, unmitigated; slight dizziness on 7th day.
++++	+++	++	+	Hamstrings and abdomen moderately relaxed; patient sleeps better.
++++	++++	++	++	Patient seemed suggestible; spasms unchanged.
++	++	0	0	Spasms unchanged; moderate dizziness on 7th, 9th and 11th days.
+++	+++	+++	+++	Weakness, blurring and severe dizziness throughout.
+++	+++	+	+	Patient asymptomatic; spasms unchanged.
++++	++++	+	+	Pitting edema of hands and feet on 5th, 7th and 9th days; spasms unchanged.
+++	+++	+	+	Patient asymptomatic, with no change in spasms
++	++	++	++	No symptoms; spasms unchanged.
+	++	0	0	Spasms worse, with weakness, on 7th, 17th and 19th days, dizziness on 15th day.
+++	++	0	0	Dubious improvement in spasms
++++	++++	0	0	No changes of any nature noted
++++	+++	0	0	Spasms generally improved; weakness on 17th and 19th days; and diarrhea on 7th day.
+	+	0	0	Questionable relief of spasms; severe weakness on 17th and 19th days; syncope on 5th day.
++++	+	0	0	Spasms markedly alleviated in all components; patient "flat" for first time.
++++	++++	0	0	No changes of any type noted
++++	++	0	0	Spasms moderately but definitely decreased; drowsiness on all days.
++	++	0	0	Patient asymptomatic; spasms unabated.
++	++	0	0	Spasms unchanged, but patient sleeps more; drowsiness on 7th, 9th and 11th days.
+++	+++	0	0	Spasms unabated; dizziness on 7th and 9th days.
++	++	0	0	No changes of any type noted
++	++	0	0	Spasms unchanged; dizziness on 7th and 9th days.
++++	++++	+	+	Excitable patient, spasms unchanged; weakness on 5th, 9th and 17th days.
+	++	+	+	Spasms seemed worse; patient asymptomatic.
+++	+++	+	0	Spasms unchanged; drowsiness on all days, weakness on 3rd, 13th and 15th days.

During the past year, we have attempted to relieve spasm by a number of methods. Prostigmine and atropine administered parenterally have not been successful. Local injection of spinal nerves with procaine or related preparations provides relief of

very short duration. Anterior rhizotomy has been performed as a last resort, the extent of nerve section depending upon the problem presented by the individual patient. Effort has always been made to carry out the simplest, safest and least destructive procedure first, anterior rhizotomy being reserved for patients not benefited by prolonged trial of the less radical methods.

Transient beneficial effects were observed to follow the intramuscular injection of aqueous curare, but were nullified by incapacitating toxic symptoms. It was believed that d-tubocurarine in oil, because of its slow rate of absorption, might provide longer lasting relief of spasms without toxic side reactions. Therefore, the present study was undertaken.

Methods

Thirty-four patients on the Paraplegia Service were selected as spastic problems. The spasms ranged from mild muscle-group twitchings of almost subclinical importance to spasticity so marked as to prevent any form of ambulation. Levels of cord injury ranged from the fifth cervical to the tenth thoracic segment. Seventeen patients had been injured by high-explosive shell fragments, and 10 by gunshot wounds, and 7 had sustained compression fractures of one or more vertebras. Nine men had suffered partial lesions of the cord, and 25 demonstrated clinical evidence of complete transections. In the average patient, spasms were first noted approximately six weeks after injury (Table 1).

The 34 patients were divided into two groups of 17 each, and an attempt was made to distribute them evenly according to the level of injury and severity of spasm. Patients in the first group were given 175 mg. (1 cc.) of d-tubocurarine in oil and wax* intramuscularly every forty-eight hours for a total of ten doses. Those in the other group were given physiologic saline solution (1 cc.) intramuscularly at similar intervals and for the same period. Two series were studied, separated by an interval of approximately two months. In the first series, 16 patients were given injections, half of them receiving the medication, and half physiologic saline solution. The second series was managed similarly with a total of 18 patients. No attempt was made to isolate those under treatment, and communication between patients of the same and different wards was unrestricted. To minimize prejudicial estimates of improvement because of previous knowledge of the medication received, neither the observer in the first series (R. A. K.) nor that in the second (D. S. B.) was cognizant of the distribution of controls or drug injections. The distribution remained unknown to the observer until all injections had been completed and his written report submitted. In each series, one nurse gave injections from beginning to end of the treatment period. Patients were told only that they were receiving "medicine for spasms." Nurses and doctors were under strict injunction to guard against elaboration of this single statement. The injections were completely prepared, and the needles attached under sterile conditions in a room separate from the main ward. To promote efficiency, ten or fifteen syringes were carried in a closed container from ward to ward. A hot-water bottle covered with a sterile towel served to maintain the d-tubocurarine in liquid state. All syringes were taped to the 1-cc. mark, the quantity of injectable material kept the same in each syringe, and the barrel and needle end covered by the nurse until the moment of injection into the gluteal region. The necessity for such elaborate precautions is demonstrated by reference to the case reports presented below.

Clinical observations by doctors, physiotherapists and nurses and subjective reports by the patients were accorded most weight in evaluation of the results obtained. Clinical estimates were based upon observation of the patients' ability to ambulate and maneuver between bed and wheelchair; response of spastic extremities to pinprick and other stimuli; and resistance of the extremities to passive motion. Each patient was questioned about the frequency, duration, severity and "sensitivity" of spasms during the periods between injections, and special care was taken to avoid leading remarks. Most patients volunteered detailed statements with as little prompting as the question, "How are your spasms?" or "Are you having any trouble?"

Results

Amelioration of spasms was apparently obtained in 7 of the 34 patients. Three of these patients were receiving curare, and 4 were receiving physiologic saline solution. The degree of estimated improvement varied, but the most marked "relief" occurred in 2 patients in the latter group. In none of the patients was improvement so marked as to justify continued administration of curare. Twenty-seven patients were unimproved, 14 of these having received curare, and 13 having received physiologic saline solution.

Pain was considered to be lessened in 3 patients—2 in the medication group and 1 in the control group. No changes occurred in the remaining 31 patients.

Toxic symptoms were frequent and misleading. Manifestations of such symptoms by patients in the control group were usually indistinguishable from the complaints of patients actually receiving curare and frequently led to incorrect estimates of the type of medication being administered.

The role played by suggestibility in therapy of this type of patient was clearly demonstrated. Intramuscular injection of d-tubocurarine in oil demonstrated no effects on spasticity that could not be

*The tubocurarine was supplied by E. R. Squibb and Sons, New York City.

duplicated with intramuscular injection of physiologic saline solution.

The following case reports are illustrative of the series as a whole:

Case 1. J. S., a 21-year-old man, was wounded January 20, 1945, by a 31-caliber bullet, which entered the left anterior triangle of the neck, emerging through the left posterior triangle. He sustained a compound, comminuted fracture of the bodies of the fifth and sixth cervical vertebras, with complete loss of all motor and sensory modalities below the level of the fifth cervical segment. Within 2 days he was able to flex the left leg, and 7 days after injury he began to regain some motor power in the upper extremities. Deep-pressure sensation returned completely below the level of the second rib. Débridement was performed 9 days after injury, but no attempt was made to visualize the dura or spinal cord. The patient developed a large sacral decubitus ulcer en route to the United States, but the neurologic status was gradually improving. Examination in September demonstrated patchy hypesthesia, which ended at the fourth lumbar dermatome on the left and the fifth lumbar and first sacral dermatomes on the right, with complete anesthesia below those levels. Motor activity returned to the left upper extremity; the right biceps was weak but contracting voluntarily, and there was fair extension and flexion of the thigh on the pelvis and the leg on the thigh in the left lower extremity. Voluntary motion was present in the right lower extremity but to a lesser extent. There was no movement of the feet or toes. Concurrently with the gradual re-establishment of voluntary motor power, approximately 2½ months after injury, the patient began to notice adductor-flexor muscle spasms. The involuntary movements lasted approximately 30 seconds and were set off by changes in position or by attempts at initiating motion in the lower extremities. Turning in bed particularly excited movements. Abdominal spasms became more and more frequent. Despite daily physiotherapy and prolonged treatment with prostigmine and aqueous curare, flexion contractures of hips, knees and ankles gradually developed. In June, 1946, because of the danger of ankylosis, a series of orthopedic procedures was carried out, including bilateral fasciotomy of the hips, bilateral adductor-longus tenotomy, bilateral triple hemisection of the Achilles tendon and left hamstring tenotomy. The lower extremities were placed in casts split over the popliteal space, and the knee flexion was slowly reduced by wedging. At the end of 1 month, both lower extremities demonstrated full range of motion, but with release from the cast, strong spasms again flexed the right leg. Brace and crutch ambulation began in August, 1946, but the patient continued to be severely hampered by spasms. Attempts by the patient to inhibit flexor spasms voluntarily in the left lower extremity began to evoke strong extensor spasms.

Ten injections of 1 cc. (175 mg.) of d-tubocurarine in oil and wax were administered in the manner described above.

There was no improvement in severity, frequency or "sensitivity" of spasm. Toxic symptoms of overdosage occurred throughout the entire course of treatment, as evidenced by blurring of vision, diplopia, dizziness, headache and weakness. Two episodes of nausea and vomiting occurred within 1 hour of injection.

Case 2. F. N., a 30-year-old man, was injured on June 9, 1945, when the truck in which he was riding plunged off a cliff in Germany. He sustained immediate complete paralysis, with a sensory and motor level at the fifth dorsal dermatome. X-ray study revealed comminuted fractures of the transverse processes and bodies of the fifth and sixth dorsal vertebras, and lumbar puncture demonstrated partial block. The patient was placed in hyperextension and returned to the United States. Onset of reflex activity was noted 1 week after injury, with the appearance of bilateral hallux dorsiflexion. One month later there was mild abdominal spasm, and within the following few weeks mild thigh flexion appeared. At 3 months he developed an extensor component, which appeared while he was lying on the side and back. The adductor-flexor type of mass reflex increased gradually in severity, and by March, 1946, the spasms were strong, usually extensor in pattern and set off by almost any stimulus. Laminectomy performed on August 14 revealed an atrophic spinal cord with cystic degeneration at the level of the fourth and fifth dorsal vertebras. Approximately one eighth of the left posterolateral column was stated to be "anatomically intact." The posterior roots of the fifth dorsal segment were severed bilaterally in an attempt to relieve the girdle pains. No change resulted except for an increase in pain at that level. Ambulation was first begun on long leg braces with a back brace in April. With the exception of the postoperative laminectomy period, the patient subsequently continued to ambulate. Flexion-adduction and extension spasms markedly interfered with walking, and the patient had reached a point beyond which he could not progress.

Ten injections of .1 cc. (175 mg.) of d-tubocurarine in oil and wax were administered in the manner described above.

No improvement was observed in the severity, frequency or "sensitivity" of spasms. Girdle pain remained the same. The patient experienced dizziness on the 5th day of treatment, and some blurring of vision on the 21st day.

Case 3. J. D., a 34-year-old man, was wounded on November 24, 1944, by a high-explosive shell fragment, which struck him in the interscapular region, inflicting a compound, comminuted fracture of the laminae and bodies of the third and fourth dorsal vertebras. There was no loss of consciousness, but immediate complete sensory and motor paralysis, distal to the third thoracic dermatome. After emergency supportive treatment, débridement was done. The dura was visualized, found to be intact and stated to pulsate well, but the cord was completely severed. Involuntary movements began approximately 1 month after injury. They first manifested themselves as mild flexion contractions involving the thighs, legs and feet. The strength and frequency of the spasms gradually became more pronounced, and 5 months after injury, lumbar, abdominal and adductor components entered the flexion picture. In September 1945, extensor thrust began bilaterally, and an extensor component, which lasted 20 to 30 seconds, appeared with marked fatigue. To date the patient has continued his efforts at ambulation. Adductor spasm and scissoring have been partially relieved by obturator neurectomy and adductor tenotomies, and it was found necessary to perform sections of both Achilles tendons to correct plantar-flexion contractures. Progress has been practically nil. Strong triple-flexion spasms, together with severe extensor spasms, have been extremely difficult to cope with. Prolonged trial with intravenous and intramuscular curare, prostigmine and atropine did not benefit the patient, and operative relief was repeatedly refused. The neurologic status and general physical condition have remained unchanged for the last ten months.

The patient was included in the control series and given ten injections of physiologic saline solution throughout the prescribed course of treatment.

On the 3rd day of treatment he thought that the extensor component of the spasm was of somewhat shorter duration than normal for him. On the 5th day the same report was given, and on the 7th day he reported and demonstrated definite relaxation of flexor, extensor, abdominal and gluteal spasms. He also reported mild diarrhea on that day, which he attributed erroneously to the medication being administered. He continued to report daily that the spasm was improving, saying, "I feel more relaxed all over" and "The spasms don't last as long, and I can bend my legs with my hands without making the spasm start — I could never do that before." On the 17th day he complained of mild weakness, but no other toxic symptoms. He felt definitely improved and repeatedly requested, after completion of the injections, that they be resumed.

Case 4. L. D., a 29-year-old man, fell 50 feet from a hangar roof on December 21, 1945, striking a concrete floor. There was immediate complete motor and sensory loss below the level of the sixth dorsal dermatome. X-ray study revealed compression fractures of the bodies of the seventh, eighth and ninth dorsal vertebras. On the following day exploratory laminectomy demonstrated complete anatomic transection of the spinal cord, with a gap between the ends, at the level of the ninth dorsal vertebra. There was considerable contusion of the cord at the levels of the seventh and eighth, and the posterior roots of the eighth and ninth

dorsal segments were lacerated. Involuntary movements were first noted by the patient approximately 6 months after injury. They began as fibrillary twitchings in the hamstrings and gradually spread to the abdominal and gluteal muscles. A triple-flexion pattern of moderate severity evolved, with occasional abduction spasms of the thighs. He was able to ambulate throughout the summer of 1946 on long leg braces with a back brace. For the past 2 months he has had extension spasms of both thighs on rising from a supine position. Bilateral plantar flexion is a part of this general pattern. The spasms usually last about 5 to 10 seconds, but may occur at any time and are more marked while he is sitting than when he is standing. Ambulation has been only moderately hindered by the involuntary activity. The main problem confronting this patient has been poor bladder control as an accompaniment of the general spasm picture. Tidal drainage was attempted in March, 1947, with no success. The bladder has a small capacity and requires frequent emptying, with no assurance that the patient will remain dry.

This patient was selected for the control series and given 1 cc. of physiologic saline solution intramuscularly every 48 hours for the usual injection period.

There was no change on the 3rd day. On the 5th day he noticed diarrhea three or four times, but there was no change in the spasms. On the 7th day he reported definite improvement in spasm frequency and severity, but complained that along with the relaxation he became dizzy, fainted and was unconscious for a period of 2 or 3 minutes. His ambulation instructor held him erect until the period of dizziness passed, but he suffered weakness and dizziness for 5 hours after the injection on that day. On the 9th day of treatment the patient stated that he was improved in all respects, with relaxation of flexor, extensor, abdominal and back spasms. The bladder was not "firing off" so frequently. He maintained this state of improvement throughout the entire course of treatment. On the 13th day he again complained of mild weakness and dizziness. He felt quite definitely that his spasms were improved and stated that they "didn't last so long." There were quite bitter complaints about the toxic symptoms he was manifesting, and because of them he wished to discontinue the injections, but was persuaded to complete the injection course. At the termination of treatment he expressed the opinion that although the spasms had been definitely improved, the fatigue and weakness accompanying injections more than counterbalanced this improvement. Accordingly, he would "rather have the spasms."

Discussion

In an attempt to evaluate the results of any medical therapy for spasms, certain limitations and difficulties must be emphasized. No objective method of measuring the degree of spasm is entirely satisfactory. Caliper or tape measurements of the range of motion possible in the spastic limb do not yield accurate data. The unpredictable and frequently abrupt "normal" variations in intensity of spasm from hour to hour are extremely confusing. It is very unusual indeed for a patient to reproduce the identical intensity and pattern of spasticity week after week. He may volunteer the information that he has recently been much less spastic than usual, but testing will demonstrate spasms that appear to be of equal or greater severity than those noted during a day when he was, by his own estimate, "jerking all the time." If the time necessary for spasm to "tire" against a given stretch is taken as an index, the same objection holds.

Normal daily variation, which is dependent upon factors not yet explained, serves to minimize the value of such measurements. Myometrograms demonstrating the action potentials of spasmodically contracting muscles are impractical for the same reason. Standardization preliminary to recording each measurement is extremely difficult, and it is virtually impossible to establish a base line for comparison of one patient with another. Still photographs, as might be expected, are misleading. It was, unfortunately, not possible to obtain moving pictures of the reflex activity in these men. Slow-motion-picture analysis of the reflex movements resulting from a standard stimulus should yield fairly accurate data.

The dosage schedule utilized in this series was arrived at after some deliberation. As with any drug, optimal therapeutic dosage and tolerance vary with each patient. Available studies indicate that a single effective dose will continue to manifest its effect for forty-eight to seventy-two hours.[11, 27–29] In administering 1 cc. of d-tubocurarine in oil every forty-eight hours, we preferred to err on the side of overdosage, with the hope that toxic symptoms would not become disabling and that the majority of patients would fall within the therapeutically effective range of the drug.

It must be realized that we were dealing with patients whose injuries had placed them in a unique psychologic situation. A profound sense of inadequacy governed their daily lives. Despite a superficial rationalization encouraged by association with similarly disabled patients, there remained in these men deep feelings of inferiority and helplessness. They had been forced to the logical conclusion that their disability was in all probability a permanent one, and that they would never become normal. But such a realization did not prevent severe conflict with the hope (usually unexpressed) that some new treatment would be found or that some miracle would occur to restore their limbs. Popular articles reporting amelioration or "cures" in almost any disability, vaguely or directly related to spinal-cord injury and its sequelae, brought immediate inquiry and demand for explanation. There was fertile ground for acceptance of ideas that are medically and surgically unsound. Suggestibility was maximal, and if the desire for improvement was of sufficient strength, "improvement" would result no matter what agent was employed.

The importance of suggestion is strikingly emphasized by the patients who were given physiologic saline solution (Table 1). The "toxic symptoms" demonstrated by 4 patients are easily attributable to suggestion, but alleviation of spasm, sufficiently marked to impress the observer, demonstrates the facility with which suggestion completely obviates clinical observation. It stresses the need for controlled trial of any new drug in these patients. It is evident that a striking reduction of spasm can be produced by suggestion in certain patients with proved anatomic severance of the spinal cord. The

psychogenic factors involved, and their relation to spasm, are complex and deserve further investigation.

It is apparent that in neither series were the observers able to estimate correctly the patients receiving d-tubocurarine (Table 1). Of the total of 34 patients, the type of injection administered was judged incorrectly in 16. Nine patients receiving curare were estimated to be receiving physiologic saline solution, and 7 of those receiving saline solution were judged to be in the curare group. It is therefore obvious that little or no therapeutic effect attributable to curare was observed.

Twenty of the 34 patients exhibited apparent effects of "overdosage" at one time or another; 11 of these received curare, and 9 received saline solution. Diplopia and pitting edema of the hands and feet (the latter a complication of curarization previously unreported*) were the only two findings noted in the curare group but absent in the control group. In the remainder of patients displaying "toxic symptoms" it was impossible to differentiate the drug group from the control group. The dizziness of the patients on curare differed in no way from the dizziness suffered by those receiving saline solution. Similarly, drowsiness and weakness proved extremely difficult to evaluate. The severity of symptoms was grossly misleading. In 3 patients (M. E. S., J. S. and L. D.) toxic symptoms were sufficiently distressing to cause us considerable anxiety. Two of these patients were receiving curare, and 1 saline solution. Despite such manifestations, it was not necessary to administer prostigmine or to discontinue injections in any patient.

The opinions of physiotherapists and physical-therapy instructors, the change (if any) in spasms, the intelligence of the patient, his adjustment to his injury and his emotional stability were factors that influenced the decision whether or not he was receiving curare. Naturally, the degree of conviction concerning the type of medication being administered varied for each patient, and in some cases a definite opinion was difficult to formulate.

Seven patients with partial cord lesions received curare, and 2 received saline solution. The preponderance of the curare group was unintentional but fortunate, since it offered an opportunity to compare results of curare in patients with paraparesis and those with paraplegia. Three of these patients were incorrectly judged to be receiving saline solution. One patient was markedly relaxed, and 1 moderately so. In the group receiving d-tubocurarine none of the patients with complete transection of the spinal cord demonstrated decrease of spasm. The reduction of spasm mentioned above might be significant except for the fact that even more pronounced relaxation occurred in some patients receiving saline solution.

A request for continuation of injections was considered a strong indication that real relief was being provided. Of those receiving d-tubocurarine, 1 patient asked that the injections be continued, whereas in the group given saline solution 2 made such a request. The 2 patients considered by the observers to be most relaxed by their injections (J. M. and H. F.) were in the group receiving saline solution. The false conviction that H. F. had been receiving d-tubocurarine was so strong that a heated argument ensued, and was resolved only by exhibition of the dosage schedule.

Of the 17 patients given d-tubocurarine, 9 were wrongly estimated to be receiving saline solution. Reference to Table 1 reveals that 5 of these men demonstrated no changes whatsoever attributable to medication. No symptoms were reported and spasms were unabated. One patient complained of intermittent weakness and diplopia. This particular patient, with an incomplete spinal-cord lesion and fair voluntary motion in both lower extremities, demonstrated the most violent and uncontrollable spasms observed on the Paraplegia Service at this hospital. He exhibited no change in spasms, and the mild symptoms of which he complained seemed paradoxical to the observer. Two other patients reported questionable toxic symptoms, with no evidence of improvement.

Seven of the patients given saline solution were incorrectly estimated to be receiving curare. In 3 this inaccuracy was based on the conviction that spasms had been definitely helped; 3 others exhibited no change in spasms but rather marked "toxic symptoms," and in the remaining patient spasms were increased but were accompanied by fairly severe "toxic symptoms."

It is apparent that no significant differences between the control group and the curare group were observed, and it is concluded that no beneficial effects relating to the relief of spasms in paraplegic and paraparetic patients were obtained by the intramuscular injection of d-tubocurarine in oil.

Summary

Thirty-four patients with traumatic lesions of the spinal cord were studied in an attempt to evaluate the use of curare in spasticity due to such injuries.

Two independent series were conducted. Seventeen patients received intramuscular injections of 175 mg. of d-tubocurarine chloride in oil and white wax every forty-eight hours for ten doses, and 17 were given an equal volume of physiologic saline solution intramuscularly throughout the same treatment period.

No beneficial effects relating to the relief of spasms in paraplegic or paraparetic patients were obtained by the intramuscular injection of d-tubocurarine in oil and white wax.

*Since this manuscript was submitted for publication, Grob et al.[33] have noted a somewhat similar phenomenon accompanying intra-arterial injection of d-tubocurarine chloride, and these investigators ascribe the edema to release of a histamine-like substance.

In neither of the injection series were the observers able to estimate correctly which patients were receiving d-tubocurarine and which were receiving saline solution.

The role played by suggestibility in therapy of this type of patient was clearly demonstrated.

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RECKLINGHAUSEN'S NEUROFIBROMATOSIS ASSOCIATED WITH INTRATHORACIC MENINGOCELE*

Report of a Case

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We have recently encountered at operation an intrathoracic meningocele in a patient with Recklinghausen's neurofibromatosis upon whom we had operated fully expecting to find a paravertebral neurofibroma. A search of the literature on the subject of anterior intrathoracic meningocele revealed an interesting association between this lesion and Recklinghausen's disease, which we believe deserves comment since this association is not generally known.

Because of its rarity anterior intrathoracic meningocele is almost never considered in the differential diagnosis of intrathoracic tumor. Groedel[1] mentions the lesion in this connection in his textbook on roentgenographic diagnosis, but otherwise we have found no similar reference. Ingraham[2] observed no anterior intrathoracic meningoceles in the extensive series reported in his monograph. Almost everyone is confident that a posterior mediastinal or paravertebral mass in a patient with neurofibromatosis is a tumor of neurogenic origin — in all probability, a neurofibroma. The diagnosis of intrathoracic meningocele has not been made before operation as far as we can ascertain, although the diagnosis can probably be made, as pointed out below.

Meningoceles presenting in the sacral region are the most frequent of all those projecting anteriorly. This subject has recently been reviewed by Coller and Jackson.[3] Anterior meningoceles may be found in the cervical and lumbar regions but less commonly than in the sacral area.

A search of the literature on the subject of intrathoracic meningocele reveals accounts of 3 cases,[4-6] to which may be added the case reported below. Two of the previously reported cases of intrathoracic meningocele were found in patients with neurofibromatosis. The addition of the following case accentuates the significance of this association.

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Case Report

A 41-year-old woman with known Recklinghausen's neurofibromatosis was first seen in consultation at the Boston Dispensary on May 14, 1947. An intrathoracic tumor had been found in thoracic roentgenograms taken at the time of a respiratory infection 10 months previously. A posteroanterior roentgenogram of the thorax demonstrated a rounded tumor in the thorax adjacent to the mediastinum in the left paravertebral region (Fig. 1), with marked widening of the sixth intercostal space and erosion of the adjacent ribs and vertebral bodies. In addition, a fairly well marked kyphoscoliosis was seen. The convexity of the scoliosis was toward the left, with its apex in the region of the sixth intercostal space. Distinct erosion of the vertebral bodies and transverse processes adjacent to the tumor (Fig. 2) was also observed.

Physical examination revealed the cutaneous lesions of neurofibromatosis and the spinal deformity previously noted. Examination of the chest was negative, as was neurologic examination. Routine laboratory tests were within normal limits. A diagnosis of paravertebral intrathoracic tumor, probably neurofibroma, was made. It was thought that a dumb-bell type of tumor with an intraspinal portion might be present, although there were no neurologic signs; widening of the sixth intercostal space suggested encroachment of the tumor in this area characteristic of the dumb-bell type.

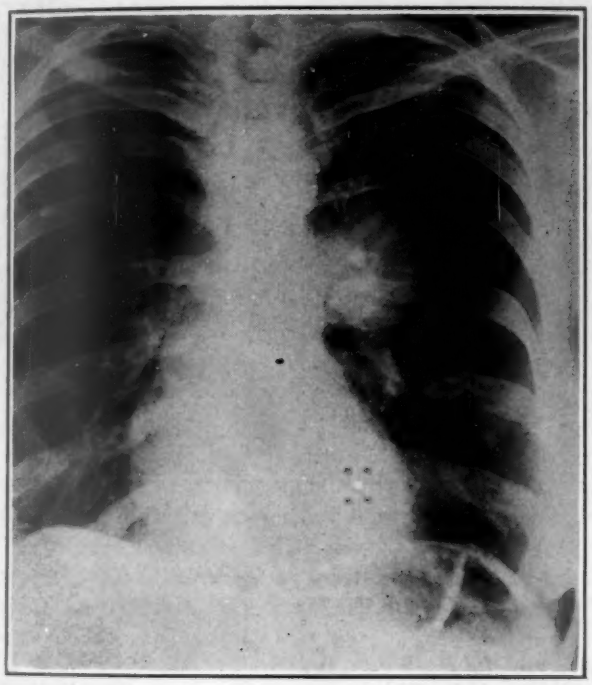


Figure 1. *Roentgenogram, Showing a Round Tumor Mass on the Left Side Projecting into the Left Lung Field at the Level of the Sixth and Seventh Ribs, with Perfectly Smooth Contours.*

There is widening of the sixth intercostal space, and there are erosive bone changes of the contours of the ribs adjacent to the mass. The findings appeared to be characteristic of intrathoracic neurofibroma.

A left posterolateral thoracotomy was performed on May 24, and the left sixth rib partially resected.

Exposure of the tumor revealed it to be a cystic mass projecting into the thoracic cavity between the sixth and seventh ribs. Its completely smooth and globular nature was evident at once. The posterior parietal pleura was incised, and the tumor was observed to be thin walled and to contain fluid. It was dissected down to its base and found to have a neck, 3 by 4 cm. in diameter, which came out of the sixth intervertebral foramen. The diagnosis of meningocele was suspected, and 250 cc. of clear spinal fluid, normal in character, was aspirated from the sac. Complete dissection of the meningocele was possible down to the leptomeninges of the spinal cord because of the great separation of the neural arches and consequent enlargement of the intervertebral foramen. The meningocele was incised, and its interior was found to be continuous with the subarachnoid space. Adequate visualization of the spinal cord was obtained. No major nerves were contained in the sac, which was excised at its neck. The dura was closed with a layer of interrupted silk sutures. To prevent the leakage of spinal fluid into the thoracic cavity, a pedicle graft of the intrinsic dorsal musculature was fashioned and sutured to the edges of the intervertebral foramen. This seemed to fit snugly and to fulfill a real need in ensuring a satisfactory support for the dural closures. The thoracic closure included the use of a steel suture for the approximation of the fifth and seventh ribs, which were widely separated because of the spinal deformity. Catheter drainage of the thoracic cavity was employed for 48 hours. Convalescence was uneventful, and the patient was discharged on the 21st postoperative day. Figures 3*A* and 3*B* show lateral roentgenograms taken before and after operation; in the latter film the previously noted area of density from the tumor is absent.

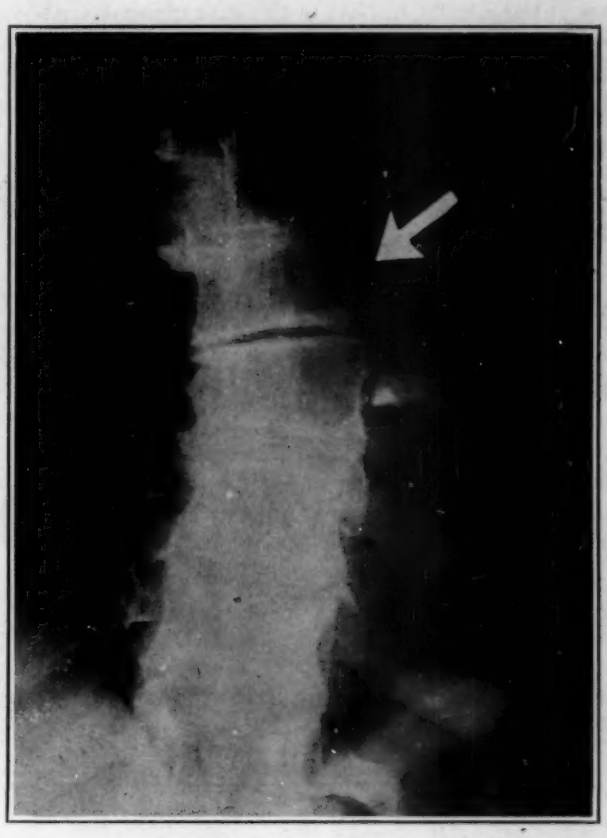


Figure 2. *Film of the Thoracic Portion of the Spine, Showing a Kyphoscoliosis with Convexity toward the Left, the Point of Greatest Convexity Being at the Level of the Sixth Intercostal Space.*

There is marked erosion of the lateral and anterior surfaces of the fifth, sixth and seventh thoracic vertebras and some erosion of the transverse processes of the sixth and seventh vertebras on the left side, together with the previously mentioned erosive changes of the ribs.

Tissue examination of the meningocele sac revealed a cyst wall composed of nerve tissue, pia arachnoid and dura showing fibrosis. The tissue findings were consistent with congenital malformation involving the three structures, nerve tissue, pia arachnoid and dura, with cyst formation.

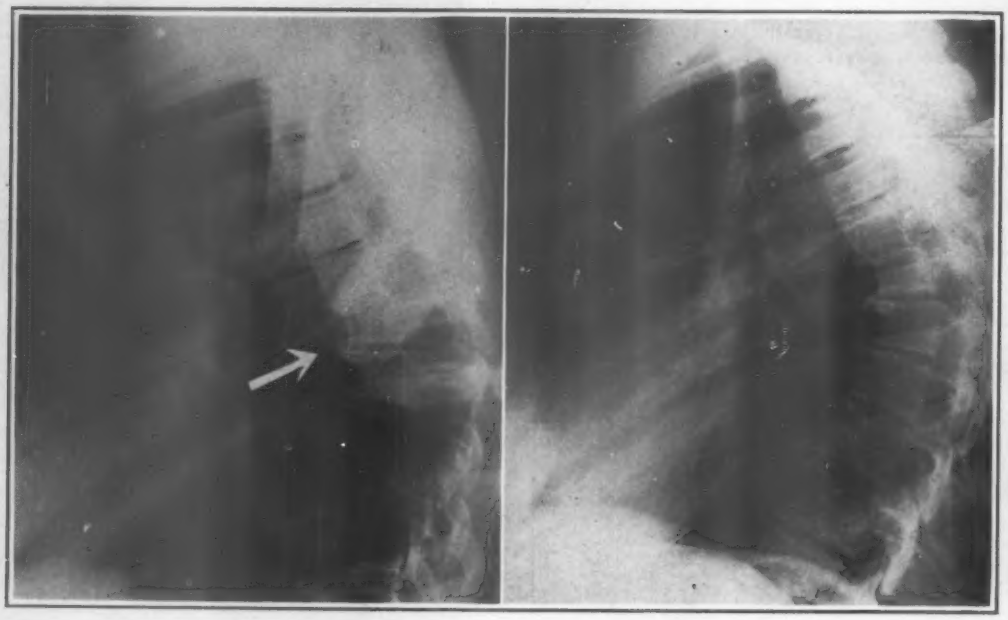
The final anatomic diagnosis in this case was simple meningocele; the wall contained portions of all layers of the leptomeninges.

Previously Reported Cases

In 1933 Pohl[4] reported the case of a forty-seven-year-old woman with Recklinghausen's disease who came to operation with a diagnosis of solid tumor of the mediastinum, probably neurofibroma. At operation a meningocele was found on the right side, which arose at the apex of a kyphoscoliosis in a manner similar to that in the case presented above. Pohl noted a high degree of widening of the intervertebral foramen and called attention to the incidence of spinal-column deformity in Recklinghausen's disease. The operative and roentgenologic findings were confirmed at autopsy, since this patient died of empyema during the postoperative period.

In 1938 Schüller and Uiberall[5] reported the findings in the case of a fifty-six-year-old man with Recklinghausen's disease and a right-sided intrathoracic tumor who came to post-mortem examination. They had previously performed myelographic studies after a suboccipital injection of lipiodol and had perhaps used the only method of diagnosis for intrathoracic meningoceles. Retention of lipiodol was noticed in a dimple at the level of the sixth dorsal vertebra, and, in addition, a spot of lipiodol was seen outside the spinal column and presumably inside the mediastinal tumor. The authors seem to have made the correct diagnosis before death. The patient died after resection of the posterior roots of the sixth, seventh and eighth dorsal nerves, performed for relief of pain. Autopsy disclosed a meningocele, which was also associated with marked kyphoscoliosis. There was considerable enlargement of the intervertebral foramen and marked erosion of the vertebral bodies.

The third case of intrathoracic meningocele that we have found in the literature was reported by Ameuille, Wilmoth and Kudelski[6] in 1940. A large intrathoracic tumor on the right side, which seemed to emerge between the eighth and ninth thoracic vertebras and to be situated paravertebrally, was discovered in a forty-eight-year-old woman. Thoracotomy was performed, and a probable diagnosis of hydatid cyst was made at the time of operation. The cyst was punctured, and the orifice packed with gauze. Death occurred from empyema and loss of spinal fluid in the pleural cavity. At post-mortem examination the cyst was identified as a meningocele, and the cause of death was attributed to loss of spinal fluid and infection of the pleural cavity. Presumably, this patient did not have Recklinghausen's disease since no mention was made of it in the report.



A B

Figure 3. *Roentgenograms of the Thoracic Area.*

The lateral view (A) *shows the mass demonstrated in Figure 1 to be situated far posteriorly, the anterior margin projecting scarcely beyond the anterior surface of the spinal column.* B *shows a postoperative film of the thorax after excision of the meningococele.*

Discussion

In the cases of intrathoracic meningocele reported in the literature it is of interest that 2 patients had Recklinghausen's neurofibromatosis and the meningocele was associated with kyphoscoliosis and seemed to arise at the apex of the deformity.

The lesion may be congenital, since it is associated with congenital anomalies. Sharpe and Young[7] found cerebral meningocele, spina bifida,

cranial defects and defects in the digits in many cases. Thannhauser,[8] in his review of Recklinghausen's disease, refers to the frequency of developmental anomalies, as do Carrière et al.[9] in their monograph on the subject. Intrathoracic meningoceles, however, have not been specifically mentioned in these reviews. The incidence of paravertebral neurofibromas with or without intraspinal segments (dumb-bell tumors) in patients with Recklinghausen's disease is not exactly known, but it is our opinion that intrathoracic tumors of neurogenic origin are not common.

Blades,[10] in a review of 109 patients with mediastinal tumors operated upon, found thirty tumors of neurogenic origin none of which, presumably, were associated with Recklinghausen's disease. In a review of a collected series of 105 cases of neurogenic tumors by Kent and his co-workers,[11] only 4 patients had Recklinghausen's disease. The relatively low incidence of intrathoracic neurofibromas in patients with Recklinghausen's disease should, therefore, bring the possibility of intrathoracic meningocele into greater prominence in the differential diagnosis. The incidence of malignant changes was 41 per cent in the cases of intrathoracic neurogenic tumors reported by Kent et al.[11] The uncertainty of the diagnosis represents an indication for operation in these patients. On the other hand, if the diagnosis of intrathoracic meningocele can be made, operation might be avoided, particularly in poor-risk patients with Recklinghausen's disease.

Intrathoracic meningoceles actually arise as lateral structures, usually projecting through the intervertebral foramens, and then pass anteriorly between the ribs to project paravertebrally into the thoracic cavity, pushing the posterior parietal pleura forward. Their course is quite similar to that of the dumb-bell shaped tumors, which project inside the spinal column, producing a compression of the cord, and into the thoracic cavity.

Naffziger and Brown[12] have called attention to the incidence of the leaking of spinal fluid into the pleural cavity after removal of dumb-bell tumors. The same complication, which may follow operation for meningoceles, was responsible for death in at least 1 of the reported cases.

It seems possible that the diagnosis of intrathoracic meningocele can be made by myelography, since Schüller and Uiberall[5] have presented evidence that meningoceles in this region can be partially filled and visualized. Eichler[13] was apparently the first to visualize an anterior sacral meningocele with this method. In patients with Recklinghausen's disease, marked kyphoscoliosis and an intrathoracic tumor, the diagnosis of meningocele should be entertained and a myelogram performed.

Summary

A case of Recklinghausen's neurofibromatosis and an intrathoracic meningocele is reported.

Of the 3 previously reported cases of intrathoracic meningocele, 2 occurred in patients with Recklinghausen's disease. The presence of intrathoracic meningocele should be borne in mind whenever one encounters a patient with Recklinghausen's disease and roentgenologic evidence of an intrathoracic tumor in the paravertebral region, particularly if there is erosion of the vertebras and ribs and kyphoscoliosis. The position and progression of meningoceles from the spinal column proceed in a lateral and anterior direction, usually through the intervertebral foramen in a manner similar to that of dumb-bell tumors. Meningoceles, however, do not produce spinal-cord compression and neurologic signs. The operative approach for intrathoracic meningoceles is transthoracic. The management of dural closure presents the same problem that exists in the removal of dumb-bell tumors. Closure of the dura must be tight, and in the case reported above, a pedicle graft of the intrinsic muscles of the back was used to reinforce the dural closure.

In the previous reports on intrathoracic meningoceles, all the patients died at operation — 1 after resection of the posterior roots of the dorsal nerves for pain, and the others after direct operative attack on the meningocele, loss of spinal fluid into the pleural cavity and empyema being the cause of death in these 2 cases.

Myelographic studies may be helpful in certain patients with Recklinghausen's neurofibromatosis and intrathoracic tumors. On the chance that a meningocele is present, the examiner should try to fill such tumors with opaque mediums by gravity and position changes during myelography in an attempt to demonstrate continuity of the tumor with the subarachnoid space. Failure to fill the tumor by either air or opaque mediums, however, does not disprove a diagnosis of anterior meningocele.

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EOSINOPHILIC GRANULOMA*

Report of a Case with X-ray Evidence of Rapid Progression

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WEST ROXBURY, MASSACHUSETTS

EOSINOPHILIC granuloma is a rare disease of bone that has only recently been described as an entity. Approximately 45 cases have been reported in the literature. The condition was simultaneously described in 1940 by Lichtenstein and Jaffe[1] and by Otani and Ehrlich.[2] The former employed the term "eosinophilic granuloma," and the latter "solitary granuloma of bone," to describe the same pathologic process. Otani and Ehrlich's term has largely been dropped, because the lesions are not always solitary and "eosinophilic granuloma" gives a connotation that adds specificity to the mental picture of the lesion. Two previous reports[3, 4] in the literature described lesions that, in the light of present knowledge, were probably the same disease as eosinophilic granuloma. It remained for these four authors, however, to collect several cases and present the clinical, x-ray and pathological picture as a distinct disease.

In 1942 Farber[5] and later Green and Farber[6] suggested that eosinophilic granuloma was not in itself a specific disease but was one phase of the progression of xanthomas that ultimately developed into Hand–Schüller–Christian's disease. They presented cases that ran the gamut from what has been described as typical lesions of eosinophilic granuloma to the clinical picture of exophthalmos, diabetes insipidus and lesions of the cranial fossa. In 1944 Jaffe and Lichtenstein[7] reviewed the subject and agreed that eosinophilic granuloma, Letterer–Siwe's disease and Hand–Schüller–Christian's disease were allied, but emphasized the inflammatory aspect. A clinical and morphologic transition from eosinophilic granuloma to Hand–Schüller–Christian's disease has been observed by Engelbreth–Holm et al.[8] in 5 cases. It is not the purpose of this paper to take sides in this controversy. There are many who agree with Green and Farber[6] that this is a metabolic dyscrasia. Others consider it to be an inflammatory disease, possibly infectious, although no etiologic agent has yet been isolated.

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CLINICAL PICTURE

Eosinophilic granuloma occurs more frequently in male than female patients. It is seen most commonly in children and young adults. About 80 per cent of the cases reported in the literature were in children. It is extremely rare over the age of twenty-five. Otani and Ehrlich,[2] in their original paper, reported a case in a thirty-five-year-old man. Versiani, Figueiro and Junqueira[9] reported a case in a fifty-year-old woman who developed a pathologic fracture in the left tibia, biopsy of which showed typical eosinophilic granuloma interspersed with areas of xanthomatous tissue. This woman in addition had diabetes insipidus, although she had no exophthalmos and no cranial defects by x-ray study. She may thus represent an in-between phase as described by Green and Farber.[6]

The disease has certain other characteristics in addition to the age and sex incidence. The lesions may be single or multiple and may involve any of the bones except those of the hands and feet. The ribs and skull, however, are the favorite sites. The long bones are next. One lesion has been reported in the clavicle.[10] X-ray films show rarefied, punched-out areas, which may erode the cortex and in which pathologic fractures may occur. New bone formation may appear secondary to these fractures. There are no associated generalized symptoms, such as fever, malaise and those referable to the gastrointestinal or cardiorespiratory system. Symptoms that are present are due entirely to the local lesion. In the case reported below there was local pain and tenderness. Certain lesions in the skull have led to somewhat bizarre neurologic manifestations.[11] Laboratory examinations are of no help in making a diagnosis. The white-cell count and the morphology of the blood cells are usually normal. Occasionally, there is a slight eosinophilia. The blood calcium, phosphorus, acid and alkaline phosphatase and cholesterol levels are normal.

Gross examination of the lesions shows soft granulation tissue, which in places is hemorrhagic, in others yellowish and in still others necrotic, frequently with some destruction and replacement by granulomatous tissue. Microscopically, there are sheets of eosinophils along with phagocytic mono-

nuclear and multinuclear histiocytes. Round-cell perivascular infiltration may be prominent.

The case reported below is interesting from two points of view. The patient, except for the woman of fifty described by Versiani et al.,[9] is to our knowledge the oldest thus far reported. What is probably of more interest are the x-ray films. In eosinophilic granuloma the duration of symptomatology is often only a few months. The disease has therefore been considered to be rapidly progressive. In no previously reported case, however, has this feature been so graphically demonstrated. In two months what originally appeared to be a small benign cyst, measuring 0.5 cm. in diameter, became a process that destroyed about 3 cm. of rib.

FIGURE 1. *X-ray Film Taken on April 1, 1946, Showing a Cystic Lesion of the Right Seventh Rib.*

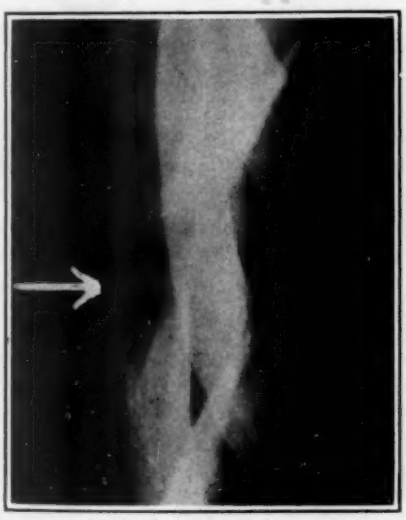

FIGURE 2. *X-ray Film Taken on April 29, 1946, Showing Erosion of the Cortex of the Rib.*

Most authors agree that although the usual treatment is local excision and curettage, the lesion can be successfully handled by small doses of x-ray therapy or even by no treatment at all.[6–11] One would have to possess considerable fortitude to have maintained a laissez-faire policy when presented with these x-ray films, not knowing what the lesion showed microscopically. It is our opinion that it is wise to perform a biopsy of any lesion before x-ray treatment or radical or conservative surgery is considered.

CASE REPORT

J. L., a 39-year-old shipper, entered the hospital on May 18, 1946, complaining of constant pain and soreness in the right anterolateral portion of the chest. About 1½ years before entry he had fallen against a truck and hurt the right side of the chest, which had been strapped with adhesive tape, and the symptoms had subsided in 1 week. He was then well until 1½ months before entry, when he was seized by a pain in the right side of the chest while lifting a heavy packing case. X-ray films taken in another clinic disclosed a small cystic lesion of the seventh rib (Fig. 1). About 4 weeks later a second x-ray film showed an increase in the size of the lesion (Fig. 2). There was no history of respiratory complaints or of any generalized symptoms. A review of the system was negative.

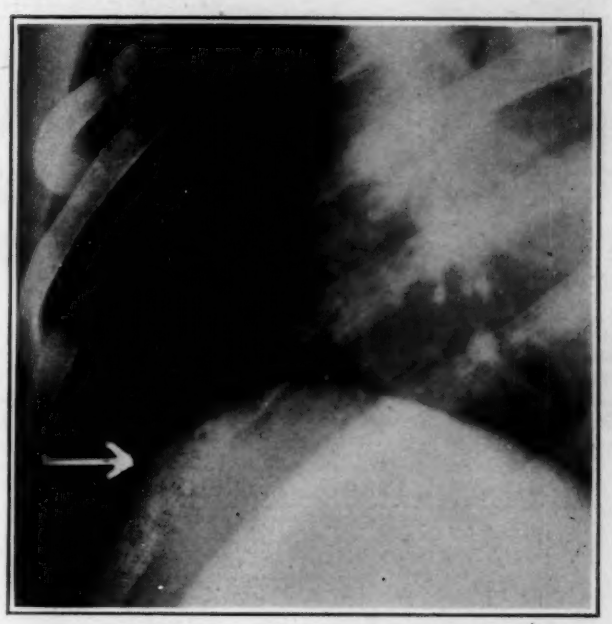

FIGURE 3. *X-ray Film Taken on May 31, 1946, Showing Marked Destruction of the Ribs in Two Months.*

The past history revealed an attack of rheumatic fever in 1925, with no early or late sequelae.

Physical examination showed a well developed and well nourished man in no acute distress but complaining of soreness in the right anterior axillary line, well localized to the seventh rib. There was moderate tenderness in this area, and a depression could be felt in the rib but no soft-tissue mass. Examination otherwise was negative.

Examination of the blood revealed a hemoglobin of 18 gm. and white-cell counts of 8600 and 9200, with 55 per cent neutrophils, 34 per cent lymphocytes, 8 per cent monocytes, 2 per cent eosinophils and 1 per cent basophils. Examination of the urine, including tests for Bence-Jones protein, were negative. A Mazzini test was negative.

X-ray films showed a great deal more destruction of the seventh rib than had been present at the examination 1 month previously. In addition there was a fracture through the

FIGURE 4. *Enlargement of Figure 3, Showing Detail of the Destructive Process.*

lesion (Fig. 3 and 4). Films of the long bones, skull and pelvis were completely normal.

While in the hospital the patient had an afebrile course. In the early part of his stay the x-ray films taken prior to

FIGURE 5. *Postoperative X-ray Film, Showing Partial Rib Resection.*

admission were not available. For this reason there was considerable discussion about the nature of the lesion presented by the physical findings and x-ray examination in this hospital. The possibilities mentioned ranged from Ewing tumor and osteogenic sarcoma to multiple myeloma, osteomyelitis and eosinophilic granuloma. When the other films became available, it was generally believed that the lesion was benign but that exploration was warranted in view of the rapid progression of the process.

On June 12, under endotracheal nitrous oxide, oxygen and ether anesthesia, a partial rib resection was carried out. On exposure of the lesion no invasion of the surrounding tissue was found. There was a pathologic fracture through the rather thin bone. Frozen section was made of the tissue obtained at operation and reported as eosinophilic granuloma. The patient made a smooth postoperative convalescence and was discharged from the hospital on June 19.

At follow-up examination 6 months later, the patient was asymptomatic. Physical examination was negative, and recheck x-ray films were normal (Fig. 5).

Pathological examination of the specimen revealed a segment of rib 7.5 cm. long, 1.8 cm. wide and 0.6 cm. thick at

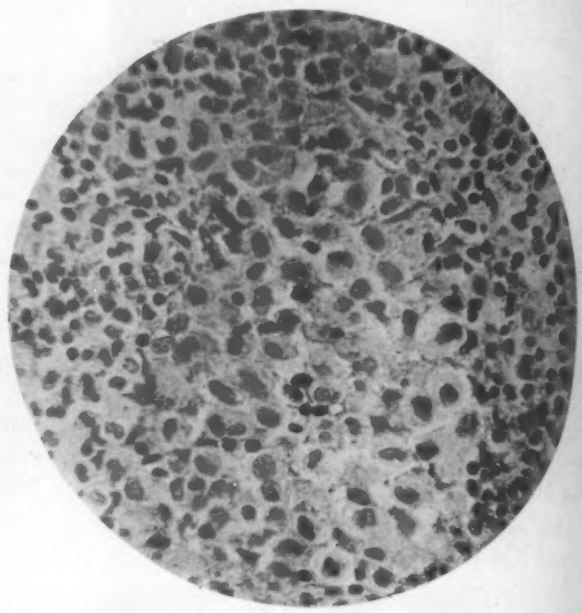

FIGURE 6. *Photomicrograph of a Typical Section, Demonstrating Eosinophilic Cells at the Periphery and Histiocytes in the Center, a Few of Which Show the Typical Indented Nucleus.*

the anterior end, and 1.5 cm. wide and 0.5 cm. thick at the posterior end. The following is a transcription of the pathological report:

> There is a slight fusiform dilatation of the central portion through which there is a transverse pathologic fracture, with loss of continuity of the bone. At the widest point the rib is 2.0 cm. wide and 1.0 cm. thick. The widened part is occupied by an almond-shaped mass of soft, gray-brown tissue, 3.1 by 1.7 by 0.9 cm in diameter, that is fairly well demarcated from the bone at the ends. Anteriorly, the cortex is completely destroyed over the mass, which is covered only by bulging red periosteum. Posteriorly, new white callus, 2 mm. or more thick, has formed over the old cortex, and appears to be infiltrated with gray-brown tissue in its inner portion. This tissue extends grossly only as far as 1.7 cm. from the anterior end and 2 cm. from the posterior end of the specimen. It perforates the cortex at the posterosuperior edge of the rib, but does not appear to pass beyond or through the periosteum at any point.
>
> Microscopical examination of the soft yellow-brown central tissue shows vascular granulation tissue containing follicle-sized foci of loosely arranged histiocytes with large pale nuclei, occasional multinucleate (giant) cells, massive infiltration with eosinophils and lymphocytes in

equal or lesser numbers (Fig. 6). There is an area of necrosis centrally. Peripherally, there is a transition into dense scar tissue with fibrous endarteritis. Perivascular lymphocytic infiltration and macrophages containing old blood pigment extend into the adjoining skeletal muscle.

The diagnosis was eosinophilic granuloma of bone (benign).

Summary

The literature on eosinophilic granuloma is briefly reviewed.

A case in a thirty-nine-year-old man is presented. X-ray films showed a very rapid progression of the disease in the course of two months.

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A SEVERE REACTION TO TETRAETHYLAMMONIUM CHLORIDE

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BOSTON

TETRAETHYLAMMONIUM salts have been found to block efferent autonomic impulses at both the sympathetic and parasympathetic ganglions.[1, 2] Because of this action, the drug is being employed in a variety of clinical studies. The effect of tetraethylammonium ion in man has been described by Lyons and his associates,[3–5] who have administered the drug over a thousand times with "very few serious effects." They make particular reference to the occasional profound fall in blood pressure and transient vascular collapse in patients with malignant hypertension who have received tetraethylammonium parenterally. Otherwise, there has been no report of a severe untoward reaction to this drug. In the course of studies on hypertensive patients and on intestinal motility at the Massachusetts General Hospital,[6] tetraethylammonium ion had been given nearly a hundred times before a severe reaction occurred. The purpose of this communication is to report the reaction in detail.

Case Report

A 37-year-old nulliparous housewife entered the hospital for the investigation of abdominal pain. She had undergone five abdominal operations for pelvic inflammatory disease, which had resulted in the cessation of menses and the occurrence of hot flashes in 1934. Several years later she began to have attacks of severe epigastric and right-upper-quadrant pain, which radiated through to the tip of the right scapula and to the right shoulder. These attacks were accompanied by nausea and vomiting. Cholecystectomy revealed an inflamed gall bladder, but no gallstones. She felt well for 18 months but thereafter continued to have episodes of pain similar to those preceding the cholecystectomy. In 1942 she was seen for the first time at this hospital, where a common-duct exploration was advised, but was declined by the patient. At that time the blood pressure was 120/70. After this admission she had infrequent pain. In 1946 frequent attacks of epigastric and right-upper-quadrant pain radiating to the right scapula and shoulder again developed. During such an attack accompanied by severe vomiting she re-entered the hospital.

Physical examination was remarkable only for an olive tint of the skin and multiple abdominal scars. The blood pressure was 110/70. Laboratory findings, including a gastrointestinal series, barium enema, intravenous pyelogram, duodenal drainage, serum amylase and all liver-function tests, were within normal limits. Because of the obscure nature of the pain, intestinal-motility studies were done by one of us (W. P. C.) using distensible balloons placed in the upper portion of the small bowel. The blood pressure previous to the test averaged 105/70. The intravenous administration of 0.6 mg. of atropine abolished the intestinal contractions and relieved the abdominal pain. The distention of a balloon immediately below the ligament of Treitz reproduced the right-upper-quadrant pain, but without its usual radiation.

On the following morning the patient was given tetraethylammonium chloride with the intestinal balloons in place, to observe the effect on the pain of abolishing intestinal contractions with this agent. Before the injection the blood pressure and pulse rate were recorded at 2-minute intervals for 10 minutes. The blood pressure averaged 120/80 and remained nearly constant. The average pulse rate was 75. The abdominal pain was then of moderate to severe intensity. Tetraethylammonium chloride, in a dosage of 230 mg., was given intravenously at a rate of 100 mg. per minute. The patient was hyperventilating slightly immediately before the injection. This increased markedly during the administration and immediately thereafter. Within 1 minute after the injection had been begun, the intestinal contractions ceased, with complete relief of pain. At that time the blood pressure was 115/85. After 230 mg. of the drug had been given, the blood pressure fell to 75/55, with a pulse rate of 80. Because of this decrease the remainder of the contemplated dosage of 300 mg. was not given. Within the next 30 seconds the patient complained of numbness and weakness, became dyspneic and pale, and then sat up, exhibiting ineffectual,

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gasping respirations of an alarming nature. She later stated that at that time a large flash of light had appeared before her, after which "everything went black." The blood pressure was 68/48, and the pulse rate 96. Epinephrine (0.2 cc. of a 1:1000 solution) was given intravenously, after which the blood pressure rose to 102/76 and the pulse rate to 108 per minute. The respiratory distress was relieved, and she felt better. Within 4 or 5 minutes the blood pressure again fell to 68/54, the respiratory distress returned, and 0.1 to 0.2 cc. of epinephrine was again given, in addition to oxygen by mask. During the next 15 minutes this sequence of events was repeated three times. Because the pulse rate rose to 140, neosynephrine was substituted for epinephrine on a subsequent occasion, and an intravenous infusion of 1000 cc. of 5 per cent dextrose in water was started. Fifteen minutes after the administration of tetraethylammonium chloride the patient complained of inability to move the legs, which persisted for 20 minutes. At about the same time she had well marked carpopedal spasm and a positive Chvostek sign, which were dispelled by rebreathing. Thirty-five minutes after the injection of tetraethylammonium chloride, intestinal contractions returned to their previous normal level. Nevertheless, the blood pressure remained at 70/40, with a pulse rate of 140. Over the next 2-hour period the blood pressure was hardly obtainable, and the patient continued to complain of marked weakness. An electrocardiogram revealed a perfectly regular rhythm at a rate of 190, which did not vary with carotid-sinus pressure. Small upright P waves immediately preceding the QRS complexes could be seen only in the special auricular Lead 3. The duration of the QRS complexes was 0.08 second, and they were of small amplitude. The ST segments were sagging in Leads 2 and 3, and the T waves were essentially flat in all conventional limb leads. These findings were interpreted as representing rapid paroxysmal auricular tachycardia. The arrhythmia persisted for 18 hours, reverting to normal rhythm at a rate of 110 per minute after a test dose of 75 mg. of quinidine lactate given intramuscularly. Throughout the acute episode the patient remained fully conscious, and the skin remained dry.

During the afternoon of this severe reaction, the patient received 600 cc. of plasma and 500 cc. of whole blood, after which the blood pressure stabilized at 90/60. Despite the reversion to a normal heart rate and rhythm, the blood pressure remained at levels averaging 80/65 on the 1st day, 80/60 on the 2nd day, and 80/55 on the 3rd day after the administration of tetraethylammmonium chloride. Subjectively, the patient gradually improved, and the blood pressure rose to 90/60 on the 9th day at the time of discharge from the hospital.

One month later the patient was readmitted for further studies, which failed to elucidate the cause of the severe reaction to tetraethylammonium chloride. During this admission the blood pressures averaged 100/65. Liver-function studies were again negative. An extensive laboratory evaluation of the endocrine status, including, among other procedures, a Wilder test, determinations of 17 ketosteroids, 11 oxysteroids, serum sodium and potassium, and inspection of the rate of axillary-hair growth, revealed values within normal limits except for a basal metabolic rate averaging −22 per cent and an elevated urinary output of follicle-stimulating hormone (the last finding was consistent with the menopausal state). The diagnoses on discharge were possible biliary dyskinesia, menopausal syndrome and psychoneurosis. At a subsequent laparotomy the common duct was normal except for a somewhat constricted sphincter of Oddi, multiple adhesions involving the upper portion of the small intestine and a dilated duodenum.

Discussion

It appears that the administration of 230 mg. of tetraethylammonium chloride given to this patient produced a severe immediate reaction, which was characterized by profound hypotension and an alarming degree of respiratory distress. The hyperventilation may have been on the basis of anxiety, but Lyons et al.[4] described 4 female patients who developed sudden hyperventilation after the administration of this drug. They also reported transient inability to move the legs, a feature that this patient presented. The persistence of hypotension for several days cannot be definitely ascribed to the drug, since the return of intestinal contractions occurred in the usual time,[6] suggesting that the tetraethylammonium ion had been largely eliminated. The paroxysmal tachycardia could be attributed to the drug, to the use of the vasopressor drugs or to the patient's unstable emotional state.

The manner in which such an unfortunate reaction to the drug may be avoided by proper selection of cases is beclouded by the many features that characterized this patient. She was a small, asthenic, emotionally unstable woman with a low-normal blood pressure, who had symptoms and laboratory evidence suggestive of the menopause and of hypothyroidism. Whatever the mechanisms involved, the fact remains that the patient experienced an untoward reaction to the administration of tetraethylammonium chloride of such severity as to cause grave concern. The possible occurrence of such a reaction is called to the attention of those using the drug or contemplating its use.

Summary

The action of tetraethylammonium chloride in man is briefly discussed, and the literature briefly reviewed.

A case of a severe untoward reaction to the drug is reported.

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MEDICAL PROGRESS

TECHNICAL ADVANCES IN PHYSICAL MEDICINE

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IN RECENT years those concerned with developments in the field of physical medicine have rightfully emphasized the need for fundamental research, and a number of investigative and training centers have been established with this in mind.[1] Reviews of current research in physical medicine have been the subject of previous reports in this series[2] and elsewhere.[3] Physical medicine is best known, however, for its therapeutic activities, and certain developments in technic constitute the basis of the following report.

PROGRESSIVE-RESISTANCE EXERCISES

Therapeutic exercise can be considered the most frequently utilized and probably the most valuable single procedure in this specialty. It is accordingly of some significance to report an advance in technic of application. DeLorme,[4] while serving in the Army Medical Corps, reported the successful adaptation of the system of muscle training of professional weight lifters to restore maximum function to weak, atrophied muscles after certain types of disease and injury.

The basic principles of this system may be simply stated. To produce power in a muscle — that is, ability to lift heavier loads — the training exercises should be with heavy resistances and few repetitions. In contrast, endurance is developed by low-resistance exercises with frequent repetitions as with stationary bicycle riding. This method of heavy-resistance, low-repetition exercising was found by DeLorme to develop muscular power to a remarkable degree, as evidenced by ability to lift greater weights and by actual muscular hypertrophy according to circumferential measurement. The speed of such muscular development was much more rapid than that observed with the conventional type of exercises.[4]

Exercise Program

The exact exercise load for any patient is based on his maximum effort as recorded once a week on the test day. At the beginning of the program weights are gradually added to the load upon the exercised muscle until the maximum that can be moved ten times through the full range of motion is determined. This is designated as the 10-repetition maximum (10 R. M.). The exercise work schedule for the following week is based on this determination.

In the original papers by DeLorme[4, 5] the work program consisted of a series of exercises, usually with seven to ten sets of different weight lifts repeated ten times each as the daily exercise stint. Exercise was started with lighter loads and ended with ten lifts at the 10-repetition maximum. Once a week on the test day the 10-repetition maximum was determined, which usually increased, and also the 1-repetition maximum (1 R. M.), or the greatest weight that could be lifted once through the full range of motion. In some cases, as in joint instability, incomplete healing of wounds or arthritis, the determination of the 1-repetition maximum was omitted. The usual weekly schedule consisted of the daily exercises with the same prescribed weights and frequencies until the test day, after which there were two days without any exercise. Only one exercise period a day was permitted.

Results

In the first series of patients reported by DeLorme emphasis was placed on development of power of the quadriceps muscle. The types of cases treated included unstable knees from tears of cruciate and collateral ligaments and after removal of the menisci, as well as fractured femurs and patellas, recurrent dislocations of the patella and atrophy of the quadriceps from prolonged immobilization from fractures in the vicinity of the knee joint or other injuries necessitating immobilization. He found that in a series of patients the average time required to restore normal power to the extensor mechanism of the knee was nineteen days. It was also observed that such heavy-resistance exercises were more satisfactory than weight-bearing exercises before full muscle strength had been regained. At the same time increase in the range of knee motion was coincident with the increase in muscular power, the range of motion closely approaching normal unless gross damage of articular surfaces was present.

This principle of relatively maximal resistance with minimal repetitions as advocated by DeLorme has been put to clinical test in a variety of conditions beyond those of trauma to bones and joints. Preliminary studies in patients with residual weakness from poliomyelitis have indicated that muscle groups previously with power of only 20 to 50 per cent of normal may be able to increase their functional capacity to a significant degree.[6] This was found true even in cases of long-standing paresis

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when careful measurement of muscle strength was made by means of ergographic tracings, maximum-effort test, spring-gauge test and circumferential measurement of muscular volume. The rapidity of improvement in muscular strength in these long-standing cases of poliomyelitis was, as might be expected, considerably slower than that in patients suffering only from weakness of disuse atrophy. It was also observed that improvement in muscle strength was not sufficient to cause an increase in grading according to the usual manual scale, although significant changes were observed in the maximum-strength tests and ergographic tracings. It was further noted that the patients reported coincident improvement in functional ability in ordinary tasks such as ability to walk greater distances without fatigue.

Physiologic Studies

As might be anticipated, this method of exercise was soon investigated by physiologists on normal persons, particularly because of the empiric origin and nature of the training regime employed. At the Baruch Center of Physical Medicine at the Medical College of Virginia a group of normal persons were subjected to a period of training with heavy-resistance exercises following the DeLorme technic involving the motions of knee extension and elbow flexion.[7] In this study the daily work unit consisted of 70 to 100 contractions divided into bouts of 10, with rest pauses between the series of repetitions as originally proposed by DeLorme, the last series not surpassing the 10-repetition maximum. The study period consisted of not less than four weeks of exercise, and the criteria of improvement were obtained by the maximum efforts put out on the test days — namely, the 10 R. M. or the 1 R. M. The results obtained suggested that the most important single element leading to increase in work output was the will to perform a physiologic maximum effort. Daily exercise of this sort was found to produce a significant increase in work done on each weekly test day, and the improvement in work capacity under such a program of heavy-resistance exercise was rapid, for strength more than doubled in four weeks of systematic training. The increased work capacity was also found to continue during a post-exercise period, which exceeded in duration the initial period of training; in fact, the ability to perform work might continue to improve after the cessation of systematic training, suggesting a type of motor learning including extension of the psychologic end point of fatigue.

Further studies of a similar nature from the same laboratory are of considerable interest.[8] In another experiment normal adults were subjected to a series of heavy-resistance exercises to a single upper or lower extremity, and the changes in the contralateral limb were observed. Such exercises, which rapidly increased the strength of the exercised limb, had a corresponding effect on the contralateral unexercised extremity, although the results were less marked. It was believed that the determining factor in this so-called "cross education" was the severity of the effort evoking the response rather than the duration of the exercise. It was suspected, however, that the unpracticed side received many reflex stimuli, which acted upon it to evoke widespread synergistical contraction. The results of this study suggested that such "cross education" might serve as a useful therapeutic tool in cases in which volitional control is unilaterally defective or in which contralateral muscle groups are rendered temporarily inaccessible through immobilization.

Technic of Exercise

Because so little detailed information is available concerning the use of this exercise equipment, particularly as applied to the weaker grade muscles, some of the important technical aspects are discussed. In relation to counterbalancing in exercises two terms must be defined: the "exercise load" and the "muscle load." The exercise load is the load that is placed upon the weight pan of the apparatus and does not necessarily refer to the resistance placed upon the muscle, since in some cases it is used as counterbalance. The muscle load is the actual resistance the muscle must overcome during the exercise. For strong muscles the muscle load includes the weight of the extremity and the exercise load. For weak muscles the muscle load is still near the maximum for that muscle but less than the weight of the extremity, for the exercise load serves as a counterbalance. When the exercise load is used as counterbalance it never exceeds the weight of the extremity, thus producing passive motion, but is always within the range necessitating maximum voluntary effort. The term "load-assisting exercises" has been applied to procedures in which the exercise load assists the muscle, and "load-resisting exercises" to those in which the load resists the muscle.

With load-resisting exercises the work increase for the week is based, as mentioned above, on the 10-repetition maximum. With load-assisting exercises the exercise routine is based on the 10-repetition minimum, which is determined by tests for the smallest load on the weight pan that still permits the muscle to perform not more than 10 repetitions while doing a load-assisting exercise. As muscle strength increases it can be seen that the exercise load will decrease. The opposite is true in case of load-resisting exercises. It has also been found when dealing with these weaker grades of muscles that the daily exercise prescription, instead of being from 70 to 100 repetitions, may be reduced to three sets of 10 repetitions or even less. An approximate scheme for determining exercise loads is as follows[9]:

Load-resisting exercises	
First set of 10 repetitions	A half of 10-repetition maximum
Second set of 10 repetitions	Three fourths of 10-repetition maximum
Third set of 10 repetitions	10-repetition maximum
Load-assisting exercises	
First set of 10 repetitions	Twice the 10-repetition minimum
Second set of 10 repetitions	One and a half times the 10-repetition minimum
Third set of 10 repetitions	10-repetition minimum

With improvement in strength it is possible simply by readjusting the pulley arrangement to change from load-assisting to load-resisting exercises, thus continuing the principle of progressive resistance exercises with near maximum resistances of few repetitions at all times (Fig. 1).

Microwaves ("Radar")

High-frequency electrical currents have been used in medicine and surgery for over fifty years. It was demonstrated, particularly by d'Arsonval, that frequencies above 10,000 cycles per second produce no evident effect beyond that of heating the tissues through which they pass. Frequencies in the neighborhood of 1,000,000 to 3,000,000 cycles per second or long-wave diathermy began to be employed about 1900 and are still in use. Over 10 years ago the frequencies were increased in clinical generators to the neighborhood of 10,000,000 cycles with a wave length of 30 meters or less (short-wave diathermy). Then frequencies of 100,000,000 cycles were produced, or wave lengths of 3 meters. They were called ultra short-waves. Electronic developments have now made it possible to apply frequencies of 3,000,000,000 cycles of wave lengths of 10 cm., which have been called microwaves and are related to radar of wartime prominence. Although radiations of such frequencies and wave lengths were produced before the war, it was not until recently that their possible usefulness in medical practice could be determined.

Physical Characteristics

Certain physical properties of microwaves can be contrasted readily with radiations of lower frequency in the radio-frequency spectrum. Microwaves have optical properties, for they can be reflected, refracted and diffracted. They can also be focused by suitable lenses and reflectors much as the beam of a searchlight. Microwaves may be selectively absorbed, but the biologic significance of this is still unknown.

This high-frequency energy cannot be transmitted from and to antennae in the usual fashion of a lower frequency but is transported along hollow pipes or coaxial cables, known as wave-guides, which must be carefully designed according to the frequency used. Certain meteorologic conditions in nature may act as wave-guides, and during the war the pulse-echo system was used to determine the location of enemy targets with radar. Therapeutically, however, energy is continuously rather than intermittently transmitted.

It has been found that the absorption factor of water at 100°F. for microwaves at a frequency of 2450 megacycles per second — that assigned by the Federal Communications Commission — was approximately seven times greater than that of the usual short-wave frequencies of 27 megacycles. There is thus experimental physical evidence of the possible efficiency of this type of energy for heating purposes, provided the output is sufficient and properly controlled and directed.

Experimental Studies

One of the first published reports on the effects of microwaves on living tissues comes from the Mayo Clinic.[10] The results of these studies on dogs indicated that microwaves were an effective heating agent. Rises of cutaneous temperature between 3 and 5 degrees were accomplished in twenty minutes with moderate output. Corresponding rises in subcutaneous and muscular tissue were also observed. Measurements of circulation were made with a bubble-flow meter that indicated increased venous return from the heated extremities. No unusual effects were observed other than those to be expected from the corresponding rises in temperatures of the tissues.

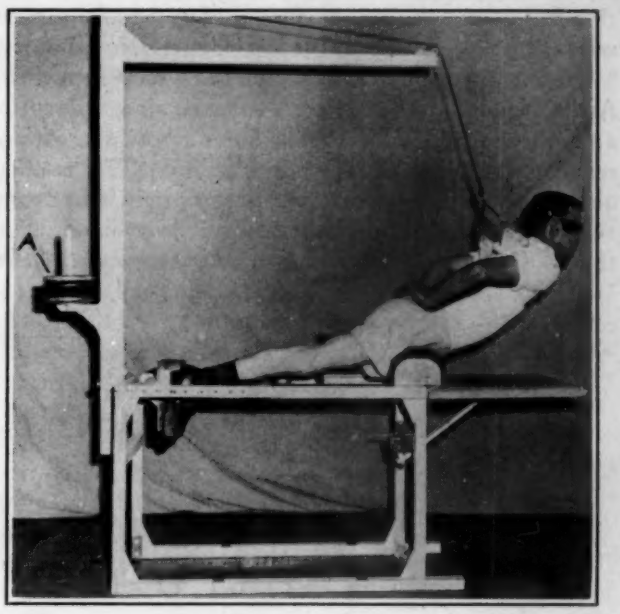

Figure 1. *Exercise for Strengthening Weak Back Muscles. Hyperextension is made possible by counterbalance* (A) *in addition to the patient's maximum muscle power.*

The Council on Physical Medicine has also investigated the microtherm generator produced by the Raytheon Manufacturing Company and has placed it in its list of accepted devices.[11] In experiments reported on human volunteers with measurements of deep-muscle temperatures it was found that increases to 103.5 to 105°F. were obtained. It was noted that the sensation of cutaneous warmth was less than that usually expected by other means of

heating to a similar degree and that, for a given degree of cutaneous irritation, the rise in deeper tissue temperatures by microwaves was much greater than that produced by radiant heat.

I have used an early model of the Raytheon microtherm* over a period of a year. It has been utilized for heating purposes in a variety of conditions in the ordinary practice of physical medicine, including subdeltoid bursitis, radial humeral bursitis, nonsuppurative tendinitis, muscle strain and contusion, and sinusitis. The usual technic of application included exposure for twenty minutes, which resulted in comfortable warming reported by the patient and increase of cutaneous temperature with mild erythema. Patients were warned about the sensation to be expected and were told to report undue warmth as with any heat treatment. No cases of blistering, burning or untoward effects were reported. An occasional patient felt increased discomfort in an acute bursitis in no wise different from that often resulting from short-wave diathermy. The results obtained are of no statistical significance, but from this period of clinical observation it is believed that this is a safe and effective means of supplying heat to a localized area when employed with similar precautions applying to the use of diathermy. The opportunity to see the skin at all times during treatment is a technical advantage in avoiding excessive heating. This new electronic development appears to be a worthy addition to the therapeutic armamentarium of physical medicine. Further physiologic and clinical studies are indicated.

*Kindly supplied by the Raytheon Manufacturing Company, Waltham.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

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CASE 34181

PRESENTATION OF CASE

A twenty-year-old housewife was admitted to the hospital complaining of lassitude and a movable lump in the abdomen.

Two years before admission the patient became pregnant and had a normal prenatal course for the first six months. At that time while at rest she had an episode of sudden severe pain low in the lumbar region, without any radiation and lasting twenty minutes. There was no dysuria, passage of stool or pain in the lower abdomen or genital region. At one other time during pregnancy she was said to have passed bloody urine. However, she had no urinalysis during pregnancy. She had pruritus vulvae and burning on urination during pregnancy. After parturition she had dizziness, which was cured by glasses. She had felt complete lack of energy and had liver injections without effect. She ate heavily but could gain no weight (the weight was 125 pounds and during pregnancy it had been 142 pounds). Occasionally she had panicky feelings and spontaneous crying spells. She noted the presence of a slightly tender, movable lump in the right lower abdomen. She complained occasionally of mild shooting pain of right-obturator-nerve distribution. For two years during evening devotion she could not kneel and then lean forward because of pain in the midlumbar region. She had mild mucoid vaginal discharge.

There was no history of tremor, palpitation or heat intolerance. Her husband had "depressive spells," and they had been separated twice. The patient had a family history of diabetes. Six members of her family had "stiffening and fixation of the lower spine."

Examination revealed a pale, well developed, well nourished woman. There was a precordial systolic thrill and a Grade III systolic murmur best heard at the apex. There was tenderness over the right costovertebral angle and a tender, firm, 3-cm. mass in the right midportion of the abdomen. The mass was considered to be in the position of a ptotic kidney or caudate lobe of liver. It did not move with respiration. The right kidney was palpable and descended to the midportion of the abdomen. The left kidney was not felt. The cervix was lacerated, and the uterus retroflexed. There was slight adnexial tenderness. Reflexes in the legs were normal.

The temperature, pulse and respirations were normal. The blood pressure was 130 systolic, 85 diastolic.

Examination of the blood showed a hemoglobin of 3.8 gm. and a white-cell count of 7800. The differential count was within normal limits. Urinalysis was negative. The lumbar spine was radiologically normal. An excretory urogram showed the kidneys to be normal in size, shape and position. The dye appeared promptly in both urinary tracts. There was no definite abnormality of calyxes and pelves. The right ureter was somewhat kinked at its upper extremity, but this caused no obstruction. A film taken in the upright position showed both kidneys to descend about 5 cm. A barium enema revealed no intrinsic abnormality or external compression. An ill defined shadow was noted on the right side of the abdomen below the right kidney partially obscuring the shadow of the right psoas muscle. Lateral films taken at another hospital showed the presence of a mass below the right kidney, displacing the ureter medially and anteriorly.

On the fifth hospital day an operation was performed.

Differential Diagnosis

Dr. Richard Schatzki*: It does not seem out of place to start with the x-ray films. We shall first look at the films taken at the other hospital, about two weeks prior to admission. The films with catheters in both ureters show the left ureter in approximately normal position and the right ureter to be displaced far medially and overlying the spine. The shadow of the left psoas muscle is clearly visible; the right is visible but not so well defined. I cannot see a definite soft-tissue mass. The right kidney is well outlined and appears normal in size and shape. After injection of dye through the catheters normal kidney pelves are seen on both sides. The right ureter still maintains its position over the spine even after the catheter has been withdrawn partially; its displacement starts at the ureteropelvic junction. The lateral film shows the kidney in normal position, but the ureter, starting at the ureteropelvic junction, seems to be displaced forward. The films taken at this hospital show again a normal-appearing kidney. The shadow of the left psoas muscle is clearly outlined; the right is outlined a little more clearly than on the films taken elsewhere. On some of the films I think I can see something that looks like a mass below the kidney, but this is by no means definite. There is disturbingly little visible to suggest a mass. The intravenous pyelograms do not outline the ureters well enough to determine their position. The upper end of the ureter on the right side shows some displacement forward as on the outside films, and we will therefore assume that the ureter had the same position as on the previous examination.

A barium enema was performed and was said to be completely normal, without displacement of the colon. It is difficult to make a statement of displacement of the intestines from films unless there are a number of them or the displacement is quite marked, and I hesitate to express an opinion about anything that is so vaguely seen, but on these films I have the impression that the ascending colon is slightly more to the right than usual. In both these films after evacuation the whole colon drops down normally; there is no fixation of the colon anywhere. Of interest is the lateral film that was taken apparently after evacuation of the enema, and the thing that impresses me is that there seems to be a difference in the size of the abdomen compared with the films taken approximately two weeks previously. I measured the distance from the anterior abdominal wall to the anterior aspect of the spine on both films, and it certainly is greater on the recent film. The patient apparently was a slender woman, and very slight changes in position of the patient may influence the measurable thickness of the abdomen. So I do not know that we are justified in taking this difference in size of the abdomen as a definite fact; otherwise, it would be extremely interesting. That is as far as we can go on the x-ray appearance.

What conclusions can be drawn from the evidence so far? The logical conclusion is that this patient had a mass in the retroperitoneal space on the right side, which displaced the right ureter forward and to the left. There are many lesions in the retroperitoneal space that can produce such a displacement. There are numerous benign tumors that may occur there, the most common one probably being a neurofibroma. Could this have been a neurofibroma? The location is consistent. The patient's history would certainly go with the diagnosis. The patient had one attack of severe pain, which is unusual. She had occasional pain in the distribution of the obturator nerve, which runs along the medial aspect of the psoas muscle in the region where the pathologic lesion appears to be. We do not see any defect in the spine. A neurofibroma anywhere near the spine, even originating from the spine, does not have to deform the spine; and certainly in the abdomen, where there is so much space for a tumor to grow, it would not cause pressure defects in the spine. There are a few disturbing features about the diagnosis of neurofibroma. The first is that I cannot see the tumor on the plain films — disturbing for a tumor of this size. The other disturbing feature is the fact that clinically the mass is described as being 3 cm. in diameter. If what was felt clinically coincides with what we believe to be the lesion in these films, the mass should be larger than 3 cm. Of course it is possible that the clinical mass represented only a portion

*Radiologist, Mt. Auburn Hospital, Cambridge, Massachusetts.

of the x-ray mass, which would go well with neurofibroma, since neurofibroma is often lobulated. Neurofibroma is still a good possibility.

What other retroperitoneal tumors may occur? There may have been a lipoma in the retroperitoneal tissue. That would explain nicely why we see so little of the tumor mass. On the other hand we do not see any radiolucency, such as one would expect from a lipoma in this location. Against lipoma is the fact that the mass was readily palpable by the patient. I would rather believe that that makes the diagnosis unlikely.

Another mass in the retroperitoneal region in that area could be a cyst originating from the kidney. Cysts may originate particularly from the lower pole of the kidney, and the kidney shadow may appear to be perfectly normal, if the cysts are pedunculated. A pedunculated cyst of the lower pole of the right kidney could produce this picture. Again, it is rather surprising that we do not see a definite mass on the plain film.

There are all kinds of other queer tumors that may occur in this location. It is an interesting embryologic region. The wolffian and müllerian ducts may leave cysts behind. There are occasional cysts of the ureter, ovarian cysts and so forth. I do not know how one can make a definite diagnosis of any of these lesions. There are other benign tumors that I am sure may occur.

We have of course the possibility of malignant tumors; metastatic cancer may occur retroperitoneally. We do not have to worry too much about this possibility since the lesion had not changed much in two years' time. I do not believe that we can rule out a slowly growing sarcoma, fibrosarcoma or neurofibrosarcoma — in other words, a tumor similar to the first tumor that I mentioned, neurofibroma, only its malignant variant.

Another tumor in this area is the teratoma. I would not try to make a diagnosis from the evidence at hand. Dermoid cyst belongs to the congenital ones that I have already mentioned.

Was this lesion necessarily a tumor? An abscess in the retroperitoneal space would produce the same displacement of the ureter. There is nothing in the history to suggest abscess. A hemorrhage into the retroperitoneal space could produce such a displacement. Again, there is nothing in the history to suggest that the patient had a hemorrhage, although I think it is possible for someone to have a hemorrhage without any dramatic clinical story to go with it. That would explain the displacement and would explain why we see so little of a soft-tissue mass. I do not believe that we can rule it out, but with the negative history it is definitely a long shot.

Is it necessary to suppose that what we see had anything to do with the patient's complaint — not the lassitude, but the lump? It is possible that what we see is a red herring and that the patient had an additional mass in the peritoneal cavity — a tumor of the small bowel 3 cm. in diameter. Displacement of the ureters may occur with other conditions than masses, as we have already said. The ureter may be pulled over by a scarring process or by loss of substance on the side to which the ureter is pulled. Again, we have nothing to suggest this course of events. It would be helpful to find something in the peritoneal cavity that would explain the free mobility of the mass. On the other hand, the free mobility was an observation of the patient; there was no statement by the doctor that the mass was movable. Some mobility is possible in retroperitoneal tumors. The normal pancreas and the normal kidney have definite mobility. Pedunculated tumors may have a good deal of mobility. You may remember a case taken up at one of these conferences in which the discusser was led astray by just this fact — a pancreatic cyst that was freely movable, which had caused the discusser to rule out a retroperitoneal mass.

We have not enough evidence on which to base the possibility of an intraperitoneal mass.

I shall make a diagnosis of retroperitoneal mass. I do not know its histology. I shall place neurofibroma first and question of cyst of the lower pole of the kidney second, but I know very well that I have no right to make a histologic diagnosis.

Dr. William A. Clark: Will Dr. Schatzki comment on whether or not the sacroiliac joints look normal. Much of the symptomatology might be explained on the basis of mild rheumatoid spondylitis.

Dr. Schatzki: I would call them normal.

Dr. Ronald C. Sniffen: Do you agree with Dr. Schatzki's reasoning, Dr. Wyman?

Dr. Stanley M. Wyman: I agree completely.

Clinical Diagnosis

Retroperitoneal tumor.

Dr. Schatzki's Diagnosis

Retroperitoneal mass:
Neurofibroma?
Cyst of lower pole of kidney?

Anatomical Diagnosis

Ganglioneuroma, retroperitoneal.

Pathological Discussion

Dr. Sniffen: Dr. Dobyns, you took care of this patient? Will you tell us what you know about her?

Dr. Brown M. Dobyns: Operation was performed by Dr. Oliver Cope. The patient was sent in in the belief that she had a tumor, probably above the kidney. The mass that was felt was thought to be the kidney. The x-ray films (retrograde pyelograms) that you have seen did not accompany the patient when she arrived. After a number of days of study she was about ready to be discharged because of lack of positive evidence that could be obtained.

Then we sent for the x-ray films, thinking that the doctor's idea that there was something in the renal region might be confirmed. The displacement of the ureter was well demonstrated in the retrograde pyelograms. Exploration was accomplished through a right transverse abdominal incision. The ascending colon was pushed forward by a mass, which was exposed by reflecting the right colon and cecum medially. The mass had several long fingers of tissue that extended upward and posterior to the vena cava, wrapping around and adherent to it. At the upper end this extended almost behind the liver. There were several secondary masses about the size of a golf ball in the connective tissue immediately adjacent to the main tumor. The whole mass was dissected out from above downward. We tied off a number of small vessels leading from the tumor to the vena cava. The mass was found to arise on a pedicle that came through a small aperture in the psoas muscle. It came through at the level of the third lumbar vertebra. This aperture is the usual anatomic pathway of the sympathetic commissure. The tumor was not adherent to the anterior branches of the lumbar plexus. It had no obvious relation to the obturator nerve or the anterior femoral cutaneous nerve, and it was thought that the tumor arose from sympathetic-nerve tissue because the sympathetic trunk was not present after removal of the tumor. The tumor was thought to have been completely removed.

Dr. Sniffen: Did you think that the neoplastic tissue had multiple points of origin or was a single lobulated tumor?

Dr. Dobyns: We believed when we removed the specimen that there was a moderate amount of freedom between the secondary tumor nodules and the main mass. They were close enough to the main mass to have had some continuity.

Dr. Sniffen: The tumor that Dr. Cope removed was a lobulated, encapsulated mass. Microscopical sections showed a dense background of nerve fibers in which ganglion cells were embedded. In short, the tumor was a ganglioneuroma. As you know, the ganglioneuroma is the most highly differentiated tumor arising from the anlage of the autonomic nervous system. Usually, it is found in the adrenal medulla or along the line of the paravertebral ganglions. Metastasis does not occur, but multiple tumors are not a rarity. In neuroblastomas, which are the undifferentiated tumors of the sympathetic anlage, one occasionally finds areas of differentiation into ganglioneuroma. I should think that the prognosis is excellent in this case.

CASE 34182

Presentation of Case

The patient was a full-term baby girl born in the hospital after a normal labor of twelve hours by a para V mother.

The pregnancy was uneventful. The mother was sedated with seconal (0.3 gm.), amytal (0.4 gm.), and scopolamine (0.4 mg.). The child was born with the cord around the neck. The body was pink, and the head blue. She was reported to have cried spontaneously. The birth weight was 6 pounds, 15 ounces, and the length was 20 inches.

The mother's third child had died shortly after birth of atelectasis.

The baby was put in an incubator and given continuous oxygen because the color was dusky. Seven hours after birth she seemed to have some difficulty in breathing. Suctioning of mucus resulted in improvement for the next four hours. At that time, eleven hours after birth, the baby, who was being observed by the nurses frequently, was found to be blue and not breathing. Suctioning of mucus and artificial respiration with oxygen by nasal catheter were carried out by the nurse and doctors who responded to an emergency call. At that time the heart rate was 50 per minute. After a few minutes the baby started to breathe, with gasping respirations, and the color improved. The heart rate likewise improved. Though the chest did not appear fully expanded, auscultation indicated satisfactory aeration. During the next few hours the baby did fairly well with nasal oxygen, but the respirations remained somewhat irregular, with intervals of apnea. A second episode of respiratory standstill and cyanosis occurred approximately six hours later. During the next two days the baby was kept in oxygen in an incubator. The color was fair, but the respirations continued irregular at times. The heart sounds were of good quality. The lungs were clear. The fontanelle was not full. There were no convulsions. Feedings were attempted, but the baby did not swallow and gavage feedings were instituted. The baby expired on the fourth day of life.

Differential Diagnosis

Dr. Ralph A. Ross: In consideration of a problem such as this, we are faced with two large groups of malformations or diseases: congenital malformations and those due to trauma during or preceding delivery or to chemical trauma from oversedation. Also, I think that we should mention, particularly because of the history of previous neonatal death in the family, transplacental sensitization producing erythroblastosis, and such esoteric infections as toxoplasmosis, which might appear during the first two or three days of life. However, there is no evidence in the subsequent course to suggest such conditions.

There are many congenital lesions that might be considered. There is a possibility of respiratory obstruction due to a lesion in the respiratory tract, such as tracheoesophageal fistula. The fact that the baby could be gavage fed with ease, rules out that possibility. A diaphragmatic hernia could

have caused the repeated spells of cyanosis. We have no evidence, however, to support that diagnosis. Cardiovascular anomalies, particularly severe lesions of the heart such as transposition of the great vessels, are frequently associated with an amazing degree of oxygenation of the peripheral blood over a period of days, and at post-mortem examination it is impossible to understand how the baby could have survived at all. We have, however, no way of determining the possibility of congenital cardiac lesions from the information at hand.

Trauma due possibly to oversedation with one of the narcotics or large doses of barbiturates, heavy intoxication with depression of the baby's centers can be a cause of this picture. However, the evidence given does not indicate that cause. Gross trauma due to the forces of labor or to the force exerted during delivery may cause hemorrhage into the subarachnoid or subdural space or from the venous sinuses subtentorially. Usually they are associated with more dramatic signs and a different course, and signs of increased intracranial pressure are commonly found. Asphyxia due to interference with the blood supply during the force of labor, because of placenta praevia, premature separation of the placenta, of which we have no evidence in this case, or pressure on the cord interfering with the baby's blood supply may very well be the cause of severe damage to the general system, with resulting petechial hemorrhages throughout many organs of the body. The brain substance itself, being more susceptible to anoxic injury, is the organ that shows most symptoms. This is borne out in the present case by the abolition of the swallowing reflex. Aspiration of amniotic fluid or mucus may be due to asphyxia; it may occur in the course of labor, and may be the cause of respiratory obstruction following delivery. Atelectasis of the lungs may be due to obstruction of the bronchioles or to inability of the baby to institute adequate respiratory motions. I think it is accepted that atelectasis is secondary, not primary, in a case of cyanosis. In the present case we have the evidence of the cord about the neck, with sufficient pressure on it to produce cyanosis of the superficial skin of the head at birth, without any cyanosis below the pressure point around the neck. We have evidence of general involvement of the central nervous system, with irregular respirations, the inability to take food and the abolition of the swallowing reflex. There were no signs or evidence of any increased intracranial pressure. We have no laboratory data to help us, owing to the fact, I assume, that the infant's condition was so precarious that any such measures as x-ray study of the chest or examination of the spinal fluid were contraindicated by that condition.

My diagnoses, therefore, are asphyxia, with diffuse petechial hemorrhages, atelectasis secondary to those, and probably some aspiration pneumonia.

Clinical Diagnoses

Asphyxia.
Cerebral hemorrhage, multiple.

Dr. Ross's Diagnoses

Asphyxia.
Diffuse petechial hemorrhage in brain substance.
Atelectasis.

Anatomical Diagnoses

Aspiration of amniotic fluid, massive.
Thrombosis of superior longitudinal sinus.

Pathological Discussion

Dr. Charles S. Kubik: I shall tell you about the findings in the brain, and Dr. Sniffen will give you the other findings. There was a thrombus in the posterior part of the superior longitudinal sinus. Some of the cerebral veins entering the sinus on the right side were greatly distended, whereas those on the left were not, and it was thought that these engorged veins were also thrombosed. There was considerable hemorrhagic extravasation in the dura and falx in the region of the superior longitudinal sinus. There were no hemorrhages within the substance of the brain or the brain stem, which on gross examination were not definitely abnormal.

We have microscopical sections of practically all parts of the brain, the brain stem and the cerebellum. It is very difficult to tell even now whether the superior longitudinal sinus and veins in question contained ante-mortem thrombi or post-mortem clots. We thought that they were probably thrombi, though very recent ones, with no reaction of the intima or the adjacent hemorrhagic dura, and certainly less than four or even two days old. It is, therefore, unlikely that these findings account to any large extent for the symptoms that were observed. The brain, mid-brain, pons and medulla were not remarkable.

DR. ALLAN M. BUTLER: That means that microscopically you found no evidence of anoxia of the brain cells?

DR. KUBIK: Nothing that seemed significant.

DR. BUTLER: No evidence of petechial hemorrhage?

DR. KUBIK: Certainly nothing striking. Small hemorrhages within the substance of the brain are not at all uncommon as a terminal event in cases in which there has been serious respiratory difficulty.

DR. ROSS: The episodes of cyanosis that were observed after birth may have been sufficient to cause some degree of petechial hemorrhage.

DR. KUBIK: They may have. Anoxia may be of a degree to cause severe disturbance of cerebral function without producing any characteristic histopathological changes. Perhaps Dr. Sniffen can throw further light on the situation.

DR. RONALD C. SNIFFEN: The gross findings in the viscera were unimpressive. There was obvious collapse of both lungs, and the liver was slightly pale. Microscopically, there proved to be a serious change in the lungs in the form of massive inhalation of amniotic fluid, which was identified by the presence of the cells of the vernix caseosa. The fluid had reached and obstructed the respiratory bronchioles and sometimes the alveolar ducts, and consequently the alveoli were not aerated. A hyaline membrane lined many of the bronchioles. The formation of the hyaline membrane is presumed to have been the result of exaggerated respiratory effort with margination of the protein precipitate within the air ducts. The liver showed quite marked fatty change, and there was a nephrosis that involved the proximal convoluted tubules. Both these changes are seen in anoxia.

DR. KUBIK: Would the changes in the lung account for the difficulty in respiration?

DR. SNIFFEN: I should think so. There was a massive aspiration, with unexpanded lung beyond the obstruction.

DR. BUTLER: I should think that the findings suggest clearly that the baby had intrauterine anoxia with accentuation of respirations and an undue aspiration of amniotic fluid and later on suffered further anoxia due to faulty functioning of the respiratory center as a result of the first intrauterine anoxia.

DR. KUBIK: I might say that it is difficult to evaluate recent nerve-cell changes in infants. Judged by standards that apply in adults the cells look diseased in almost every case. In this case it may be said that there was no actual loss of nerve cells and no findings that would justify a diagnosis of anoxia. That would have to be made on the basis of the clinical manifestations.

DR. BUTLER: How long is the period before such changes result in necrosis?

DR. KUBIK: In localized lesions resulting from arterial occlusion in adults there are well defined and distinct changes within fifteen hours and probably less. They would be more difficult to recognize in a diffuse process and against a background of terminal changes.

DR. ROSS: Why should the infant have had loss of swallowing reflex? The post-mortem findings do not explain it.

DR. KUBIK: There may be serious derangement of function in a nervous structure that cannot be recognized histologically.

DR. BUTLER: The baby's respirations were typical of the respiration that results from anoxic damage to the respiratory center.

DR. KUBIK: In our experience with human beings changes that we can recognize do not occur unless there has been loss of consciousness. Even then remarkably little may be found in some cases. In a case of carbon monoxide poisoning the patient had been unconscious for a number of hours and then lived for several days, finally dying of a pulmonary embolus. There were two small patches of degeneration, and nothing definitely abnormal in the rest of the brain.

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THE LABORER AND HIS HIRE

THE task that faces the organized profession of medicine, the hospitals, hospital and medical service organizations and Government itself in determining the destiny of medical care constitutes one of the uppermost problems of the day. So great a cloud of witnesses is involved in any discussion of the problem that it is difficult to see clearly the issues involved and place them in their proper relation to one another.

Perhaps not of paramount importance but nevertheless particularly vexing have been the difficulties encountered as a result of Blue Cross payment of certain professional services rendered within hospitals and the relation between hospitals and staff physicians in certain branches of medicine. The criticism has been made by these staff physicians, — anesthesiologists, pathologists and roentgenologists in particular, — who may be on full-time or part-time salaries, that employing hospitals have made a profit on their salaries and that Blue Cross, by arbitrarily including their services in its coverage, has classified the product of their training and experience as a hospital rather than a professional service.

They have thus been classed, it appears from their contention, with the clerks of a store or the employees of an industry from whose earnings a legitimate profit might be expected.

In an attempt to evaluate any grievance that any party may have, the purposes of professional organization should be clearly defined. It may be assumed that the first object of all medical organization is to provide the patient with the best possible care. A second legitimate object is to assure for the physician a decent and dignified standing in his community and a living commensurate with his ability and its industrious employment.

It is admitted that Blue Cross has blundered; it is apparent also that some hospitals have erred in failing to establish proper relations between staff and administration. The mistake is common when businessmen, occupied chiefly with balance sheets, have jurisdiction over institutions that are staffed by professional men jealous of the ethics and etiquette of their profession. Even the physician turned director is too often found, at least in the eyes of his former colleagues, worshiping the golden calf instead of heeding the commandments written in stone.

A committee was appointed by the Council of the Massachusetts Medical Society in the spring of 1947 "to define hospital services and medical services and to establish the proper relations between physicians and hospitals." This committee, composed of representatives of the anesthesiologists, the pathologists and the roentgenologists, the Blue Cross, the Blue Shield, the Hospital Association and the Massachusetts Medical Society, labored long and faithfully during the hot and humid summer that ensued. It brought in a unanimous report that has so far been unimpeachable and that defined as medical hospital services those "other than ad-

ministrative, rendered by a registered physician directly to or in behalf of an individual patient for the obtainment and interpretation of data, including consultation and advice, for the diagnosis, treatment and prevention of disease."

These services, specifically, were defined as embracing "the general and special practice of medicine, surgery and obstetrics, and the practice of the related specialties including anesthesiology, physical medicine, radiology, pathology and clinical pathology. . . ."

A basic principle recommended in the report was that each department (so far as possible) be self-supporting and that *neither the hospital nor the physician rendering the service should exploit the patient or each other*. The basis of financial arrangement, however, might be salary, commission, fees or any other method that would best meet the local situation.

Certain questions are not easily answered. Is a nurse anesthetist, operating under a doctor's orders, acting as his agent in a nurse's capacity or is she engaged in the practice of medicine? The point is open to debate. May a chemist, conducting his own clinical laboratory, perform an analysis and report the result to the physician submitting the material, if he does not presume to make a diagnosis? The organized pathologists believe not, but here, again, there is room for disagreement.

So long as organized medicine uses its organization for the benefit of the patient and the improvement of its own standards and public relations, well and good. If, however, its collective power should be used, as could easily happen, to protect its members against reasonable, honest and decent competition even from without the profession, it is treading dangerously close to the less attractive paths of trade unionism.

If the profession of medicine, blinded by its cloud of witnesses, closes its eyes to the fact that there are at least two reasonable sides to nearly any argument, it is simply blocking the very progress within its ranks that it is most desirous of promoting.

Status quo is but the eye of the hurricane and cannot prevail for long. Change is inherent in all human undertakings. The wrong of today may be the right of tomorrow. When the people of a nation have had their minds made up, either by themselves or by some accepted agency, they usually get eventually what they want or what they have been persuaded to think they want.

ARMY MEDICAL RESEARCH

WAR is no longer characterized by small battles between professional armies for limited objectives. Whole populations are now involved, and the stake is nothing less than national survival. Indeed, the survival of a civilization may well be at stake in some future conflict. This broader concept of war vastly increases the responsibilities of the physician. It will no longer be enough for him to relieve the fighting troops of their sick and wounded or give medical care to the civilian population. He must do these things in time of war by all existing means, but in time of peace he must work to improve known methods and to discover methods never known before.

A recent address by Lieutenant Colonel Alfred P. Thom, M.C., chief of the Army Medical Research and Development Board, throws further light on this subject. It is good to know that the medical departments of the armed forces are keenly aware of the importance of basic research in the production of discoveries leading to major scientific advances, without which applied research alone would often be sterile. To give an idea of what the medical man is up against, a few of the most urgent problems are cited as examples: development of new physical and mental standards for the most efficient use of manpower; development of principles and psychiatric technics to prevent psychiatric casualties in war; prevention and care of casualties due to or complicated by radiation sickness and radiation burns; cold-weather operations, including preselection of personnel for Arctic service, prevention and treatment of injuries due to cold and evacuation aspects of Arctic warfare; bacterial warfare — discovery and development of defensive measures against all known and suspected disease agents; and improvements in traumatic surgery, in control of common disabling diseases, in antibiotics and in technics of immunization.

When it is remembered that a future war may make no distinction between combatants and noncombatants, the figures for the Army in the last war will give an idea of what the magnitude of the medical problem may be. Between January 1, 1942, and August 31, 1945, approximately 17,000,000 men were hospitalized, and 773,000 more men were required, directly or indirectly, to give them medical care. Thus with 10,000,000 men mobilized, at least 1 out of 10 was out of action each day either as a patient or as required for patient care. This was with the best health, disease and injury treatment record of any army in history. It is anticipated that, with widespread use of atomic and other new weapons in a future war, a much greater proportion of personnel and resources will have to be used for patient care, and the proportion of sick and injured may be much higher. How much higher the actual figure could be is suggested by the present population figure of 145,000,000. One other figure — also in the millions — is of immediate interest, and that is the annual budget of the Army Medical Research Program. It is just over $3,000,000.

Colonel Thom's closing words need no comment or elaboration:

> Every medical graduate should make it his business to be acquainted with the significance of sickness and injury in military campaigns and their possible influence on national survival, so that, if medical risks are taken, the advice given to those responsible for leadership will be such that the odds are carefully considered to give the best chances for success. In total war as never before experienced in the past, a superior, progressive army medical service and staff are fundamental requirements for winning a war. The effect on morale of inadequate care of sick and injured, as well as losses in manpower due to these causes, may be catastrophic. No citizen with medical training can consider himself a disinterested onlooker in medical problems involved in national defense. Your city may be the one chosen as a military target. We must have a superior, integrated, civil and armed force medical service if the nation is to survive. Every medical graduate must actively participate in this service and do his or her part.

NEW ENGLAND DOCTOR AND HIS PUBLIC

THE Council of the New England State Medical Societies continues to perform one of its most important functions. Organized in 1945 "to bring about a closer co-operation between the State Medical societies in New England in the development and maintenance of the highest standards in the conduct and administration of medicine, and in the furtherance of plans to improve the health of all the people in the New England States," it has added to this purpose the establishment of sound relations between the medical profession and the public.

On Sunday, March 7, 1948, despite winter and bad weather, approximately seventy-five Council members and other interested persons gathered at the Copley Plaza Hotel to engage in a discussion on The New England Doctor and His Public. Most of those present being physicians, "not snow nor rain . . . nor gloom of night" stayed them from the completion of this particular appointment.

Dr. Arthur H. Ruggles, of Providence, president of the Council, presided. Talks were given on the value of radio as a public-relations agency by James S. Powers, director of the Yankee Network Institute; on the doctor and his medical society as sources of news by Maurice Cronan, city editor of the *Hartford Courant*, and Gerald E. McLaughlin, managing editor of the *Rutland, Vermont, Daily Herald*; and on the doctor's role in community programs by Dr. Hugh R. Leavell, professor of public-health practice at Harvard University School of Public Health. These addresses were discussed by Dr. John F. Conlin, director of medical information and education of the Massachusetts Medical Society, James G. Burch, director of public relations of the Connecticut State Medical Society, and Dr. Robert O. Blood, former governor of New Hampshire.

The relations between the medical profession and the news-dispensing agencies are at present and have always been poor. The doctors, according to Mr. Powers, still dwell in their ivory tower of seclusion, still maintaining a public-be-damned attitude so far as the divulging of any news is concerned. This opinion was concurred in by the newspaper editors on the program, although definite signs of improvement are making themselves manifest — such as the very meeting at which these sentiments were expressed.

It is time for the mystery and magic in medicine to be finally and completely abolished. The public should be given the opportunity of learning about

medicine all that it can assimilate within the limits of its nonmedical education. The recent controversy over the Nolen–Miles Pound Bill has shown how sadly this information has been lacking.

At the same time the press and its public must realize that many of the confidences reposed in the doctor are in the nature of privileged communications and that he is in honor bound to respect them. They must realize that matters having to do with health and disease must be reported faithfully and interpreted accurately, and must be freed from sensationalism.

If the doctor is slow to expose himself to reportorial fire it is because he has sometimes been burned by it. There is no question that his public relations need improving, but the improvement must be on a mutual basis.

PEDIATRICS

A RECRUIT is welcomed into the swelling ranks of medical journalism with the appearance of *Pediatrics*, the new official organ of the American Academy of Pediatrics. *Pediatrics*, as a journal owned by the Academy, replaces in its relation to that society *The Journal of Pediatrics* that had been published in the interest of the Academy under the proprietorship of the C. V. Mosby Company. The latter journal continues its independent course, with Dr. Borden S. Veeder, of St. Louis, as editor.

The new journal, the first issue of which appeared in January, 1948, is edited for the Academy by Dr. Hugh McCulloch, of St. Louis, and a representative board of well known pediatricians. The first issue contains a Salute by Dr. Allan M. Butler, of Boston, the presidential address, given in December, 1947, by Dr. Lee Forrest Hill at the annual meeting of the American Academy of Pediatrics in Dallas, Texas, and a variety of scientific and clinical articles. A useful addition to the usual method of publication of papers is a summary of each in Spanish.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

HAUPTMANN — Alfred Hauptmann, M.D., of Newton Center, died on April 5. He was in his sixty-seventh year.

Dr. Hauptmann received his degree from Universität Heidelberg Medizinische Fakultät, Baden, in 1905. He came to the United States in 1939. He was a member of the staff of the Boston Dispensary, Joseph H. Pratt Diagnostic Hospital, and was medical director of the Bosworth Hospital.

His widow and a daughter survive.

SCHULTZ — Philip E. Schultz, M.D., of West Newton, died on April 3. He was in his thirty-eighth year.

Dr. Schultz received his degree from Creighton University School of Medicine, Omaha, Nebraska, in 1933. He was a member of the American Society of Anesthetists, Incorporated.

His widow survives.

NEW HAMPSHIRE MEDICAL SOCIETY

DEATHS

LADD — Samuel T. Ladd, M.D., of Portsmouth, died on March 27. He was in his seventy-second year.

Dr. Ladd received his degree from Dartmouth Medical School in 1900. He was a former president of the New Hampshire Medical Society and was a member of the New Hampshire Surgical Society.

Three sons survive.

RICHMOND — Allen P. Richmond, M.D., of Hingham, died on March 17. He was in his eighty-eighth year.

Dr. Richmond received his degree from Bellevue Hospital Medical College in 1889. He was a life member of the New Hampshire Medical Society.

A son and two daughters survive.

MEDICOLEGAL ABSTRACT

Hospitals — Standard of care required in the operation of the hospital pharmacy. The conduct of the modern hospital requires the operation of many related activities in connection with the hospitalization of patients. Interesting questions arise regarding the standard of care in the operation, supervision and maintenance of such activities as pharmacies, cafeterias, x-ray rooms, orthopedic gynmnasiums and special appliance shops. One case that sometimes arises is the accidental substitution of a dangerous medication for a similar-appearing but harmless drug. A recent Connecticut case involved such a problem.

A hospital maintained a pharmacy in the basement consisting of a workroom and a separate supply room. Boric acid and dextrose, which look alike, were purchased from the same concern in containers of similar cylindrical size and shape. A cylinder of each was kept on the floor of the pharmacy proper separated from each other by about four feet. The only distinguishing marks on the cylinders were the names of the medications and the additional words in small type on the boric acid container: "for ex-

ternal use only." Boric acid is a poison and may be fatal to newborn babies if taken internally.

Under hospital routine newborn infants were given a feeding of 5 per cent dextrose solution. On this occasion the maternity ward sent the dextrose bottle to the pharmacy to be refilled, and it was filled with boric acid, whose use in the formula resulted in the death of five babies and in injuries to a sixth. Since the hospital employed a registered pharmacist and there was apparently no negligence in his selection, it was not liable for any negligence of the pharmacist under the charitable immunity rule that prevails in Connecticut. The plaintiff, the administrator of the estate of one of the deceased babies, sought to recover, therefore, on the grounds that the hospital itself was negligent in failing to provide proper facilities, safeguards and surroundings in the pharmacy. The hospital, on the other hand, argued that it had established its pharmacy in accordance with standard practice, so that if there were any negligence involved in this respect, it was negligence on the part of the pharmacist to whom the hospital had properly delegated the job of running the pharmacy. The issue, therefore, was not whether the pharmacist or some other employee was negligent in using the wrong bottle, but whether the use of the wrong bottle resulted from a violation by the hospital management itself of a duty, which it could not delegate to subordinates, to provide certain safeguards against such mistakes in the operation of its pharmacy.

The trial court instructed the jury that certain duties were duties of the hospital and could not be delegated. In describing the extent of these nondelegable duties, the trial court said:

> This includes the duty to make provision for the inspection and use of all drugs, food, equipment, and appliances, and the report of anything unusual, uncommon or serious if, and insofar as, and to the extent that you find the making of such provision is involved in its corporate function of exercising reasonable care, in view of the functions of the hospital, and the dangers reasonably to be anticipated in their performance.

The jury returned a verdict for the plaintiff, but on appeal it was set aside and a new trial ordered. The judge's instruction to the jury was described as "entirely too broad a statement because it made the most trivial duties in connection with the running of the hospital non-delegable and possible bases of liability. If applied, it would practically eliminate the doctrine of charitable immunity of a hospital."

The court further stated:

> The trial court should not have submitted the question whether defendant failed to provide proper facilities and safeguards in the pharmacy to the jury. All of the evidence was to the effect that the pharmacy was set up in accordance with standard practice, and there was no evidence to the contrary. No written rules for its conduct had been prescribed, and there was no evidence that standard practice required this or that their existence would have changed the situation. The motion to set aside the verdict should have been granted.

> In view of this conclusion, there is little in the appeal from the judgment which requires mention. The foregoing discussion negatives the claim of the defendant that charitable immunity protects a hospital even against true corporate negligence.

True corporate negligence has been defined by the Connecticut court in another case (*Evans* v. *Lawrence and Memorial Hospitals*, 50 Atl. 2d. 443, 1946) as negligence on the part of the board of trustees acting as a board, or on the part of the executive committee of the hospital acting as such a committee within the scope of its authority. Such negligence ordinarily is in the selection of doctors, servants or employees and is a basis for liability in a number of states besides Connecticut.

This decision turns on the extent of the doctrine of charitable immunity in the particular state. In Massachusetts, on similar facts in the case of *Roosen* v. *Peter Bent Brigham Hospital* (235 Mass. 66) the substitution of corrosive sublimate for epsom salts — drugs that closely resemble each other and were kept in near proximity to each other in the pharmacy — and on an action to hold the hospital for corporate negligence in the selection of servants, the court stated:

> If a hospital is to be held responsible for negligent treatment of patients, there seems to us to be no sound ground for distinction between the negligence of the managers of the hospital and the negligence of subordinate servants as a basis for liability. A sound ground for distinction between exoneration from liability for the negligence of managers and that of subordinate servants seems equally wanting. Since it is settled that there is no liability for negligence of the latter, it must follow that there is none for that of the former. . . . The inevitable result of our own decisions is to relieve a hospital from liability for negligence of the managers in selecting incompetent subordinate agents, as well as for the negligence of such subordinate agents selected with care.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS

The May schedule for Consultation Clinics for Crippled Children in Massachusetts under the provisions of the Social Security Act follows:

Clinic	Date	Clinic Consultant
Salem	May 3	Paul W. Hugenberger
Lowell	May 7	Albert H. Brewster
Gardner	May 11	Carter R. Rowe
Haverhill	May 12	William T. Green
Brockton	May 13	George W. Van Gorder
Springfield	May 18	Garry deN. Hough, Jr.
Pittsfield	May 19	Frank A. Slowick
Worcester	May 21	John W. O'Meara
Fall River	May 24	David S. Grice
Hyannis	May 27	Paul L. Norton

Physicians referring new patients to clinics should get in touch with the district health officer to make appointments. Patients are seen by appointment only.

MISCELLANY

BOSTON CITY HOSPITAL ALUMNI ASSOCIATION

The Boston City Hospital Alumni Association held its sixtieth annual reunion and dinner at the Harvard Club of Boston on April 24.

The conspicuous event of the evening was the presentation of the newly established Major General Leonard Wood award to Dr. Elliott P. Joslin. This award will be given to distinguished members of the Association who have achieved fame in medicine or surgery.

CORRESPONDENCE

RESTORATION OF LICENSE

To the Editor: At the meeting of the Board of Registration in Medicine held April 8, it was voted to restore the registration to practice medicine in this Commonwealth to Dr. Mary E. Bolger, formerly of Worcester.

H. Quimby Gallupe, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

SERUM JAUNDICE

To the Editor: In the March 25 issue of the *Journal*, under the heading of "Idiopathic Hyperlipemia," Hopgood cited the history of a twenty-six-year-old man with this condition. The patient was first admitted to the hospital on December 11, 1946, when various tests were performed, among them being blood chemical determinations. He was discharged and was readmitted two months later for further study, but immediately started to run the classic course of hepatitis. The author states that "the jaundice . . . is believed to have been a simple infectious hepatitis."

The course of events that occurred in the case reported has subsequently been repeated many times. In the past year or two, it has been increasingly distressing on active ward services, where many venepunctures or injections are given, to have the patients return in two or three months with hepatitis. Although no blood or blood products are administered in these cases, their incubation periods justify their inclusion in the category of homologous serum jaundice. The virus is transmitted from an asymptomatic carrier or an active case to the hospital patient under investigation by the agency of improperly cleaned syringes or needles. A drop of serum remaining in a syringe is all that is necessary to infect a new victim. Because of this situation, every puncture of a patient's skin, whether for blood sugar, white-cell count or to introduce penicillin, poses a potential threat to an already sick person unless certain precautions are taken.

Individual syringes and needles should be used whenever practicable; certainly, in cases of infectious hepatitis, this is most desirable. If this measure cannot be carried out, all syringes should be thoroughly washed and needles stiletted and rinsed. For the time being, autoclaving remains the preferred method of sterilization.

These precautions are simple and well worth the trouble in view of the increasing incidence of "hospital hepatitis."

Martin C. Rosenthal, M.D.

115 Central Park West, New York 23, New York

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Office Treatment of the Eye. By Elias Selinger, M.D., attending ophthalmologist, Mt. Sinai, Cook County and Michael Reese Hospitals. 8°, cloth, 542 pp., with 67 illustrations. Chicago: The Year Book Publishers, Incorporated, $7.75.

The Thematic Apperception Test: The theory and technique of interpretation. By Silvan S. Tomkins, Ph.D., research associate, College Entrance Examination Board, and visiting lecturer in clinical psychology, Princeton University. With the collaboration of Elizabeth J. Tomkins, B.A. 8°, cloth, 297 pp. New York: Grune and Stratton, 1947. $5.00.

Handbook of Psychiatry. By Winfred Overholser, M.D., Sc.D., superintendent, St. Elizabeths Hospital, and professor of psychiatry, George Washington University School of Medicine, Washington, D. C., and Winifred V. Richmond, A.M., Ph.D. 8°, cloth, 252 pp. Philadelphia: J. B. Lippincott Company, 1947. $4.00.

Diagnosis in Daily Practice: An office routine based on the incidence of various diseases. By Benjamin V. White, M.D., assistant clinical professor of medicine, Yale University School of Medicine, consultant in gastroenterology, Veterans Administration Hospital, Newington, Conn., branch section chief in gastroenterology (New England), Veterans Administration, and assistant visiting physician and chief of Gastroenterologic Clinic, Hartford Hospital; and Charles F. Geschickter, M.D., professor of pathology, Georgetown University School of Medicine, consultant in pathology, United States Naval Medical School, Bethesda, Maryland, consultant in pathology, Mt. Alto Veterans Administration Hospital, Washington, D. C., and pathologist-in-chief, Gallinger Municipal Hospital, Washington, D. C. 8°, cloth, 693 pp., with 360 illustrations and 104 tables. Philadelphia: J. B. Lippincott Company, 1947. $15.00.

Nutritional Disorders of the Nervous System. By John D. Spillane, B.Sc., M.D. (Wales), M.R.C.P. (Lond.), assistant physician and neurologist, Cardiff Royal Infirmary. With a foreword by George Riddoch, M.D., F.R.C.P., physician to the London Hospital and to the National Hospital for Nervous Diseases, Queen Square, London. 8°, cloth, 280 pp., with 103 illustrations. Baltimore: The Williams and Wilkins Company, 1947. $5.00.

Stereoscopic Atlas of Neuroanatomy. By H. S. Rubinstein, M.D., Ph.D., director, Alfred Ullman Laboratory for Neuropsychiatric Research, Sinai Hospital, Baltimore; and C. L. Davis, M.D., professor of anatomy, School of Medicine, University of Maryland. 8°, paper, 19 pp., with 43 plates. New York: Grune and Stratton, 1947. $10.00.

Trichomonas Vaginalis and Trichomoniasis. By Ray E. Trussell, M.D., associate in hygiene and preventive medicine. With an introduction by E. D. Plass, M.D., professor of obstetrics and gynecology, State University of Iowa College of Medicine. 8°, cloth, 277 pp., with 19 illustrations and 16 tables. Springfield, Illinois: Charles C Thomas, 1947. $6.00.

Ear, Nose and Throat: Symptoms — diagnosis — treatment. By George D. Wolf, M.D., assistant clinical professor of otolaryngology, New York Medical College. 8°, cloth, 523 pp. with 149 illustrations. Philadelphia: J. B. Lippincott Company, 1947. $10.00.

Diseases of the Heart and Circulation. By Albert A. F. Peel, M.A., D.M. (Oxon.), F.R.F.P.S.(G.), professor of medicine, Anderson College of Medicine, Glasgow, and assistant physician, Victoria Infirmary, Glasgow. *Oxford Medical Publications.* 8°, cloth, 398 pp., with 61 illustrations. London: Oxford University Press, 1947. $9.75.

Calcific Disease of the Aortic Valve. By Howard T. Karsner, M.D., and Simon Koletsky, M.D., Institute of Pathology, Western Reserve University, and the University Hospitals of Cleveland. 8°, cloth, 107 pp. Philadelphia: J. B. Lippincott Company, 1947. $5.00.

Biochemistry of Cancer. By Jesse P. Greenstein, head biochemist and chairman, section on biochemistry, National Cancer Institute, National Institute of Health, United States Public Health Service, Bethesda, Maryland. 8°, cloth, 389 pp., with 39 illustrations and 104 tables. New York: Academic Press, Inc., 1947. $7.80.

The Psycho-analytical Approach to Juvenile Delinquency: Theory: case-studies: treatment. By Kate Friedlander, M.D. (Berlin), L.R.C.P., L.R.C.S. (Edin.), D.P.M. (London), Hon. psychiatrist, Institute for the Scientific Treatment of Delinquency, and clinical director, West Sussex Child Guidance Service. 8°, cloth, 296 pp. New York: International Universities Press, 1947. $5.50.

The Oculorotary Muscles. By Richard G. Scobee, M.D., instructor in ophthalmology, Washington University School of Medicine, St. Louis. 8°, cloth, 359 pp., with 112 illustrations. St. Louis: The C. V. Mosby Company, 1947. $8.00.

Blood Derivatives and Substitutes: Preparation, storage, administration and clinical results including a discussion of shock, etiology, physiology, pathology and management. By Charles S. White, M.D., Sc.D., chief of surgery, Doctors Hospital, consultant to Garfield Hospital, Providence Hospital, and Columbia Hospital, Washington, D. C., and to U. S. Naval Hospital, Bethesda, Maryland; and Jacob J. Weinstein, M.D., associate in surgery, School of Medicine, George Washington University, associate in surgery at Gallinger Municipal Hospital and George Washington University Hospital, Washington, D. C. 8°, cloth, 484 pp., with 195 illustrations. Baltimore: Williams and Wilkins Company, 1947. $7.50.

Medicine for Moderns: The new science of psychosomatic medicine. By Frank G. Slaughter, M.D. 8°, cloth, 246 pp. New York: Julian Messner, Inc., 1947. $3.50.

Reading and Visual Fatigue. By Leonard Carmichael, Ph.D., president, Tufts College, and director, Tufts Research Laboratory of Sensory Psychology and Physiology; and Walter F. Dearborn, M.D., Ph.D., director, Psycho-Educational Clinic and professor of education, Harvard University. 8°, cloth, 483 pp., with 103 illustrations and 6 tables. Boston: Houghton Mifflin Company, 1947. $5.00.

The Echo. By Lilia Van Saher. 8°, cloth, 255 pp. New York: E. P. Dutton and Company, Incorporated, 1947. $2.75.

Dermatology in General Practice. By Sigmund S. Greenbaum, M.D., professor of clinical dermatology and syphilology, University of Pennsylvania Graduate School of Medicine, dermatologist, Philadelphia General Hospital, Eagleville Sanatorium, Philadelphia Psychiatric Hospital, Bamberger Seashore Home, Atlantic City, Betty Bacharach Home, Atlantic City, Rush Hospital, and Camden General Hospital, and consultant dermatologist, Mt. Sinai Hospital. 4°, cloth, 889 pp., with 846 illustrations. Philadelphia: F. A. Davis Company, 1947. $12.00.

Clinical Neuro-Ophthalmology. By Frank B. Walsh, M.D., F.R.C. (Ed.), associate professor of ophthalmology, The Johns Hopkins University. 4°, cloth, 1532 pp., with 384 illustrations. Baltimore: Williams and Wilkins Company, 1947. $15.00.

Hodgkin's Disease and Allied Disorders. By Henry Jackson, Jr., M.D., assistant professor of medicine, Harvard Medical School, and associate physician, Thorndike Memorial Laboratory, Boston City Hospital; and Frederic Parker, Jr., M.D., associate professor of pathology, Harvard Medical School, and pathologist-in-chief, Boston City Hospital. Oxford Medical Publications. 4°, cloth, 177 pp., with 15 plates. New York: Oxford University Press, 1947. $6.50.

Congenital Malformations of the Heart. By Helen B. Taussig, M.D., associate professor of pediatrics, Johns Hopkins University School of Medicine, and director of the Children's Cardiac Clinic at the Harriet Lane Home of the Johns Hopkins Hospital. 4°, cloth, 618 pp., with 177 illustrations. New York: The Commonwealth Fund, 1947. $10.00.

Practical Office Gynecology. By Karl J. Karnaky, M.D., assistant professor of clinical gynecology, Baylor University College of Medicine, gynecologist to Jefferson Davis Hospital, Houston, Texas, and director of Menstrual Disorder Clinic, Jefferson Davis Hospital. 4°, cloth, 261 pp., with 113 illustrations. Springfield, Illinois: Charles C Thomas, 1947. $7.50.

Jaundice: Its pathogenesis and differential diagnosis. By Eli R. Movitt, M.D., acting chief of medicine, Veterans Administration Hospital, Oakland, California. 8°, cloth, 261 pp., with 22 illustrations and 34 tables. New York: Oxford University Press, 1947. $6.50. *Oxford Medical Publications.*

Surgical Treatment of the Abdomen. Supervising editor, Frederic W. Bancroft, M.D. Associate editor, Preston A. Wade, M.D., associate professor of clinical surgery, Cornell University Medical College, clinical professor of surgery, New York Medical College, attending surgeon, City Hospital of New York, and associate attending surgeon, New York Hospital. 4°, cloth, 1026 pp., with 457 illustrations and 3 color plates. Philadelphia: J. B. Lippincott Company, 1947. $18.00.

Textbook of Human Physiology. By William F. Hamilton, Ph.D., professor of physiology, University of Georgia School of Medicine. 8°, cloth, 504 pp., with 121 illustrations. Philadelphia: F. A. Davis Company, 1947. $6.00.

Transactions of the American Association of Genito-Urinary Surgeons. Fifty-seventh annual meeting held at Stockbridge, Massachusetts, June 20, 21 and 22, 1946. Volume XXXVIII. 8°, paper, 305 pp. Saint Paul: The Bruce Publishing Company, 1947.

NOTICES

ANNOUNCEMENT

Dr. Samuel H. Marder announces the removal of his office to 311 Commonwealth Avenue, Boston.

JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston
Lecture Hall, 9–10 a.m.

MEDICAL CONFERENCE PROGRAM

Wednesday, May 5 — Neuro-anatomic Mechanisms Underlying Vertigo and Nausea. Dr. Benjamin Spector.

Friday, May 7 — Renal Tuberculosis. Dr. Roger C. Graves.

Wednesday, May 12 — Pediatric Clinicopathological Conference. Drs. James M. Baty and H. E. MacMahon.

Friday, May 14 — Zinc Content of Whole Blood in Normal People and in Patients with Blood Dyscrasias. Dr. John G. Gibson, 2nd.

Wednesday, May 19 — Human Heredity with Special Reference to Mediterranean Anemia. Dr. Isadore Ludwin.

Friday, May 21 — Problems Relating to Bacterial Resistance. Dr. Tom Fite Paine, Jr.

Wednesday, May 26 — Non-Specific Urethritis. Dr. Lewis W. Kane.

Friday, May 28 — Some Actions of Folic Acid Conjugates and Antagonists on Malignant Tumors. Dr. Sidney Farber.

On Tuesday and Thursday mornings from 9 to 10 Dr. S. J. Thannhauser will give medical clinics on hospital cases. On the second and fourth Friday afternoons of each month therapeutic conferences will be held from 2 to 4 with round-

table discussion, Dr. R. P. McCombs, moderator; Dr. Merrill Sosman will conduct x-ray conferences from 4 to 6. On Saturday mornings from 9 to 10 clinics will be given by Dr. William Dameshek. Medical rounds are conducted each weekday except Saturday by members of the staff from 12 to 1.

All exercises are open to the medical profession.

TUFTS MEDICAL ALUMNI LECTURE

The annual medical alumni lecture will be given at Tufts College Medical School on Wednesday, May 5, at 4 p.m.

Dr. Daniel L. Lynch, M '07, medical director of the New England Telephone and Telegraph Company, will speak on "Problems of Industrial Medicine."

Physicians and medical students are cordially invited.

BOSTON UNIVERSITY SCHOOL OF MEDICINE ALUMNI ASSOCIATION

The annual alumni meeting and scientific program of Boston University School of Medicine will be held in the auditorium of the medical school on Friday, May 7.

PROGRAM

10:00 a.m. Observations on a Sympathetic Blocking Agent, Dibenamine. Eben H. Dustin, Boston University School of Medicine, Class of 1950.

10:15 a.m. Experimental Treatment of Anaphylactic Shock. John C. Davis, Boston University School of Medicine, Class of 1950.

10:30 a.m. Hormonal Reactivity in the Schizophrenic. Dr. William Malamud.

11:00 a.m. Treatment of Acute and Chronic Osteomyelitis. Dr. Louis G. Howard.

11:30 a.m. The Management of Infected Wounds. Dr. Chester Howe.

12:00 noon. The Ulcer Problem, with Particular Reference to the Effect of Various Surgical Procedures on Gastric Secretion. Dr. Reginald H. Smithwick.

12:30 p.m. Informal luncheon. Medical-school campus.

2:00 p.m. The Cancer Program at Boston University School of Medicine. Dr. Henry M. Lemon.

2:30 p.m. The Activities of the Tumor Clinic at the Massachusetts Memorial Hospitals. Dr. Thomas J. Anglem.

3:00 p.m. The Treatment of Streptococcal Infections with Penicillin. Dr. Louis Weinstein.

3:30 p.m. Recent Advances in Chemotherapy of Hypertension. Dr. Edward D. Freis.

In the Ball Room, Hotel Statler, the reunion and cocktail hour will be held from 5:30 to 7:00 p.m., and the dinner at 7:00 p.m.

HARVARD MEDICAL SOCIETY

A meeting of the Harvard Medical Society will be held in the amphitheater of Building D, Harvard Medical School, on Tuesday, May 11, at 8:15 p.m. The Department of Biology of the Massachusetts Institute of Technology will present a symposium entitled "Methods and Results of Tissue Ultrastructure Analysis."

PROGRAM

Ultraviolet Microscopy and Spectroscopy (Including Low Temperature Spectroscopy). J. R. Loofbourow.

Polarized Light and Electron Microscopy. F. O. Schmitt.

X-ray Diffraction. R. S. Bear.

SOUTH BOSTON MEDICAL SOCIETY

The annual dinner of the South Boston Medical Society will be held at the Harvard Club of Boston, 374 Commonwealth Avenue, on Wednesday, May 12, at 6:30 p.m. The guest speaker will be Dr. Joseph P. Lynch.

NORFOLK DISTRICT MEDICAL SOCIETY

The annual meeting of the Norfolk District Medical Society will be held at the Hotel Kenmore, Boston, on Wednesday, May 12.

PROGRAM

5:15 p.m. Business meeting. Embassy Room.

6:00 p.m. President's reception, social hour and cocktail party.

7:00 p.m. Annual dinner. Crystal Ball Room. (Dr. Karl T. Compton will speak on the subject "Some Lessons from the Story of the Atomic Bomb.")

The price of the dinner, including cocktails, is $4.00.

NORFOLK DISTRICT WOMAN'S AUXILIARY

The annual meeting of the Woman's Auxiliary of the Norfolk District Medical Society will be held in the Silver Room, Hotel Kenmore, Boston, on Wednesday, May 12, at 5:15 p.m. This meeting, which will be held concurrently with that of the Norfolk District Medical Society, will afford the last opportunity of the season for the welcome of new members and for the discussion of plans for the coming year. A cocktail hour and reception will follow the business meeting. At 7:00 p.m. the members of the Auxiliary will join their husbands for the annual dinner.

NEW ENGLAND SOCIETY OF ANESTHESIOLOGISTS

A meeting of the New England Society of Anesthesiologists will be held in the Bigelow Amphitheater of the White Building, Massachusetts General Hospital, on Tuesday, May 11, at 8:00 p.m. A scientific program entitled "Lahey Clinic Night" will be presented.

PROGRAM

Sympathetic Block — Indications and Contraindications. Dr. Robert B. Orr.

Hemolytic Transfusion Reactions. Dr. M. J. Nicholson.

Circulatory Emergencies. Dr. Edwin R. Ruzicka.

The Anesthesiologist and the Hospital Staff. Dr. Urban H. Eversole.

Physicians and medical students are invited to attend.

MASSACHUSETTS COLLEGE OF PHARMACY

Alpha Chapter of Rho Pi Phi Fraternity of the Massachusetts College of Pharmacy, with the co-sponsorship of Boston University School of Medicine, Massachusetts Medical Society, Massachusetts Dental Society and Massachusetts State Pharmaceutical Association, will present the following lectures in Hayden Memorial Hall, Boston University, on Thursday, May 13, at 8:30 p.m.: "Religion and Modern Science," by Joshua Loth Liebman, LL.D., rabbi of Temple Israel, Boston; and "Modern Advances and Medical Progress," by Morris Fishbein, M.D., editor of the *Journal of the American Medical Association*.

Admission is free. Tickets may be obtained from the Massachusetts Medical Society, 8 Fenway, Boston 15, Massachusetts.

MASSACHUSETTS TUBERCULOSIS LEAGUE, INC.

The annual meeting of the Massachusetts Tuberculosis League, Inc., will be held at the Hotel Sheraton, Boston, on May 20. Dr. James E. Perkins, of New York, newly appointed managing director of the National Tuberculosis Association, will speak on the subject "Tuberculosis Associations in the Future." Dr. Vlado A. Getting, Commissioner, Massachusetts Department of Public Health, will lead a panel discussion on "What to Do for the Sanatoriums." Dr. Alton S. Pope, director, Division of Tuberculosis, Massachusetts Department of Public Health, will lead a discussion of "Progress of General Hospitals in Chest X-ray Studies of All Patients."

INTERNATIONAL CONGRESSES ON TROPICAL MEDICINE AND MALARIA

The fourth International Congresses on Tropical Medicine and Malaria and the first to be held since 1938 will convene in Washington, D. C., from May 10 to 18. The Congresses will be held under the auspices of the Department of State, and of over sixty nations to which invitations have been extended, thirty-three have already accepted and will send official delegations.

MEDICAL VETERANS OF WORLD WAR II

An organizational meeting of physicians who served in World War II will be held at the Boston Medical Library on Thursday, May 13, at 8:00 p.m. The purpose of the proposed organization is to form a democratic group of physicians for the advance and protection of the medical profession in general and of the physician-veteran in particular.

Such an organization is particularly appropriate at the present critical time, and every physician who is a veteran of the recent war is urged to attend. Please notify friends who may be eligible.

Further information may be obtained from Kenneth A. Brown, M.D., 442 Walnut Street, Newtonville (Telephone BIgelow 4-0394).

CHILDREN'S HOSPITAL ALUMNI ASSOCIATION

The annual meeting and dinner of The Children's Hospital Alumni Association will be held at the Hotel Beaconsfield, Brookline, on Wednesday, June 2, at 6:30 p.m. A short business meeting will be held, but the evening will be devoted mainly to social activities. Mr. Bradford Washburn will show colored films on Alaska.

Before the meeting a clinicopathological conference will be held in the amphitheater of the Peter Bent Brigham Hospital from 12:00 m. to 1:00 p.m., and a clinical meeting and presentation of cases will be conducted in the amphitheater of The Children's Hospital from 2:00 to 4:30 p.m.

LASKER AWARD

The 1948 Lasker Award of $1000 for outstanding service in mental hygiene will be presented for a recent significant contribution to the education of the physician in the psychologic aspects of the practice of medicine (by "physician" is specified the nonpsychiatric medical practitioner), it was recently announced. The work of the candidates for the award must have been accomplished or generally accepted during the past year or two. Presentation of the award will be made at the annual meeting of the National Committee for Mental Hygiene on November 3 and 4 in New York City.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Thursday, May 6

Friday, May 7

*9:00–10:00 a.m. Renal Tuberculosis. Dr. Roger C. Graves. Joseph H. Pratt Diagnostic Hospital.

10:00 a.m. Annual Alumni Meeting. Boston University School of Medicine.

*10:00 a.m.–12:00 m. Medical Staff Rounds. Peter Bent Brigham Hospital.

Monday, May 10

*12:00 m. Clinicopathological Conference. Margaret Jewett Hall, Mt. Auburn Hospital, Cambridge.

Tuesday, May 11

*12:15–1:15 p.m. Clinicoroentgenological Conference. Peter Bent Brigham Hospital.

*1:30–2:30 p.m. Pediatric Rounds. Burnham Memorial Hospital for Children, Massachusetts General Hospital.

*8:00 p.m. New England Society of Anesthesiologists. Bigelow Amphitheater of the White Building, Massachusetts General Hospital.

8:15 p.m. Harvard Medical Society. Amphitheater of Building D, Harvard Medical School.

Wednesday, May 12

*9:00–10:00 a.m. Pediatric Clinicopathological Conference. Drs. James M. Baty and H. E. MacMahon. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. Grand Rounds and Clinicopathological Conference. (Children's Hospital.) Amphitheater, Peter Bent Brigham Hospital.

*2:00–3:00 p.m. Combined Clinic by the Medical, Surgical and Orthopedic Services. Amphitheater, Children's Hospital.

5:15 p.m. Norfolk District Medical Society and Woman's Auxiliary. Hotel Kenmore, Boston.

6:30 p.m. South Boston Medical Society Annual Dinner. Harvard Club of Boston.

*Open to the medical profession.

April 30 and May 1. American Gastro-Enterological Association. Page 456, issue of March 25.

May 1. Suffolk District Medical Society. Page 543, issue of April 8.

May 3. American Society for Clinical Investigation. Page 456, issue of March 25.

May 3 and 4. Association of American Physicians. Page 492, issue of April 1.

May 4. Suffolk District Medical Society. Annual Meeting. Page 582, issue of April 15.

May 4 and 5. Association of Military Surgeons of the United States. Page 456, issue of March 25.

May 5. New England Obstetrical and Gynecological Society. Page 614, issue of April 22.

May 5. Tufts Medical Alumni Lecture. Page 647.

May 5–28. Joseph H. Pratt Diagnostic Hospital. Medical Conference Program. Page 646.

May 6. Suffolk Censors' Meeting. Page 344, issue of March 4.

May 6–8. American Association for the Study of Goiter. Page xiii, issue of July 31.

May 7. Boston University School of Medicine Alumni Association. Page 647.

May 10–18. International Congresses on Tropical Medicine and Malaria. Notice above.

May 11. Harvard Medical Society. Page 647.

May 11. New England Society of Anesthesiologists. Page 647.

May 12. South Boston Medical Society. Page 647.

May 12. Norfolk District Medical Society. Page 647.

May 12. Norfolk District Woman's Auxiliary. Page 647.

May 12–14. American Association of Genito-Urinary Surgeons. Skytop Lodge, Skytop, Pennsylvania.

May 13. Indications for the Use of Forceps. Dr. Roy J. Heffernan, Pentucket Association of Physicians. 8:30 p.m. Haverhill.

May 13. Massachusetts College of Pharmacy. Page 647.

May 13. Medical Veterans of World War II. Notice above.

May 16–22. American Board of Obstetrics and Gynecology, Inc. Page 344, issue of March 4.

May 16–23. International College of Surgeons. Page 136, issue of January 22.

May 17–19. American Ophthalmological Society. Page 492, issue of April 1.

May 17–20. American Urological Association. Hotel Statler, Boston.

May 17–20. Association for the Study of Internal Secretions. Page 492, issue of April 1.

May 17–20. American Psychiatric Association. Page 614, issue of April 22.

May 18–22. American Association on Mental Deficiency. Copley Plaza Hotel, Boston.

May 20. Massachusetts Tuberculosis League, Inc. Page 647.

May 20–25. American Board of Ophthalmology. Page 170, issue of January 29.

May 23–28. American Physiotherapy Association. Page 543, issue of April 8.

May 24–26. American Gynecological Society. Page 543, issue of April 8.

May 25–27. Massachusetts Medical Society. Annual Meeting. Hotel Statler, Boston.

May 27–29. American Surgical Association. Page 455, issue of March 25.

June 2. Children's Hospital Alumni Association. Notice above.

June 3–6. American Orthopaedic Association. Page 614, issue of April 22.

June 7–10. National Gastroenterological Association. Page 455, issue of March 25.

June 14–16. American Neurological Association. Page 582, issue of April 15.

June 17–20. American College of Chest Physicians. Page 455, issue of March 25.

June 20 and 21. American Radium Society. Page 543, issue of April 8.

June 21 and 22. American Society for the Study of Sterility. Page 384, issue of March 11.

June 25 and 26. Christian Medical Society. Page 492, issue of April 1.

June 28–30. American Academy of Pediatrics. Hotel Schroeder, Milwaukee, Wisconsin.

July 6–24. Students' International Clinical Congress. Page 455, issue of March 25.

July 12–17. First International Poliomyelitis Conference. Page 36, issue of January 1.

August 11–21. International Congress on Mental Health. Page 344, issue of March 4.

August 23–26. International Society of Hematology. Page 419, issue of March 18.

August 26–28. American Association of Blood Banks. Page 420, issue of March 18.

September 7–11. American Congress of Physical Medicine. Page 582, issue of April 15.

(*Notices concluded on page xiii*)